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MALE PSEUDOHERMAPHRODITISM: SOME ENDOCRINOLOGICAL AND PSYCHOSEXUAL ASPECTS*†

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THE term male pseudohermaphroditism is applied to individuals with testes whose congenital anomalies of the external genitals result in confusion of their sex. Complete hypospadias, when it is associated with hypoplasia of the phallus, cryptorchidism, and bifid scrotum or labioscrotum, commonly results in the certification of female sex at birth and in subsequent rearing of the individual as a girl. A diagnosis of male pseudohermaphroditism does not require gynecomastia or female internal genitals. Histopathology of the testes in cryptorchidism without other genital anomalies and in male pseudohermaphroditism is similar. Congenital anomalies of the external genitals may confuse the sex of an individual, even when there is no cryptorchidism.

Since the majority of male pseudohermaphrodites are certified as females and are reared accordingly, a consideration of this subject lies well within the scope of gynecology. The majority of these patients eventually consult gynecologists and, in most instances, the verification of their gonadal status may be attributed to gynecologists. Practical and psychologically correct handling of these individuals is a gynecologic responsibility. The consensus at present is

1

that individuals with gynecoid psychosexual desires and orientation should have these trends furthered by appropriate surgery and by estrogenization. This point of view is in striking contrast to one formerly held: ascertain the nature of the gonads and then fashion the individual as best possible to fit the gonadal sex, regardless of the individual's wishes or possible psychosexual trauma. This surgical approach, although it is objective and academic, ignores environmental, social, and psychological components. It results in far more traumatism to the majority of patients than the simple expedient of accepting the sex certified on the birth certificate and requiring that the individual conform to it.

Material

Male pseudohermaphroditism is more frequent than the various isolated medical reports indicate. Kozoll[1] in 1942 collected reports of 52 cases, 19 without Müllerian derivatives and 33 with Müllerian derivatives.

This study is based upon 11 selected patients with diagnoses of male pseudohermaphroditism. Selection of these patients required adequate histopathological studies of the testes and/or satisfactory determinations of urinary gonadotropins and 17-ketosteroids. Few of the patients reported in the literature have had these special urinary hormonal studies.[2-6]

The scope of this present report is restricted. It does not embrace detailed records of these patients nor is it concerned with details of gynecologic or andrologic surgery. It is the purpose of this study to consider levels of pituitary and gonadal functions, to correlate these with testicular histopathology, to examine the endocrine homeostasis of these patients, to consider psychosexuality in relationship to the endocrine homeostasis, and to evaluate somatic as well as psychosexual responses of individuals with gynecoid orientation who were treated by castration and estrogenization. A consideration of the converse approach, efforts to further the android status of individuals with male orientation, lies beyond the scope of this study. Subsequent reports by some of us will complement the data of this study and add consideration of other aspects of male pseudohermaphroditism.

Protocols of Patients

CASE 1.—The sex of this patient, aged 4 years, 9 months, had been certified as male, but complete hypospadias with chordee, a bifid empty scrotum, and a questionable vaginal pouch caused doubt as to the real sex.

Operative Findings.—Exploratory laparotomy showed a broad ligament-like structure with unfused Müllerian tubes. Gonads without Wolffian appendages were attached to the broad ligament. Both gonads were biopsied.

Histopathology of Testes.—The testes were of fetal character with epithelial cords and lack of definite basement membranes save condensations of mesenchymal cells. The cells of the epithelial cords were not well differentiated. The interstitial tissue had a rich cell content of mesenchymal character.

Treatment.—Plastic construction of the urethra and orchidopexy are planned at a later date, unless a gynecoid trend develops, despite verification of sex at this early age.

CASE 2.—The sex of this patient, aged 14 years, had been certified as female and the patient had been reared accordingly. The clinical data of this patient were supplied by Dr. Frank Lock, Bowman Gray School of Medicine, Winston-Salem, N. C. Urinary hormone studies and histopathology were done by us. There were a hypoplastic phallus with hypospadias, and empty bifid scrotum, a rudimentary vaginal pouch, bilateral inguinal gonads and moderate gynecomastia of one year's duration.

Urinary Hormones.—Preoperative values were urinary gonadotropins 12 R. U. U. per 24 hours (3 times average normal) and urinary 17-ketosteroids 6.68 mg. per 24 hours (moderately low).

Operative Findings.—Exploratory laparotomy showed no pelvic female organs. The inguinal gonads and their epididymides were removed.

Histopathology of Testes.—The architecture was essentially normal save for some clumping of normal-appearing Leydig cells. The tubules were of normal size and the majority showed arrest of spermatogenesis at the primary spermatocyte stage. Some of the tubules contained only spermatogonia and Sertoli cells. There was no hyalinization of the tubules or thickening of the basement membranes (Fig. 1).
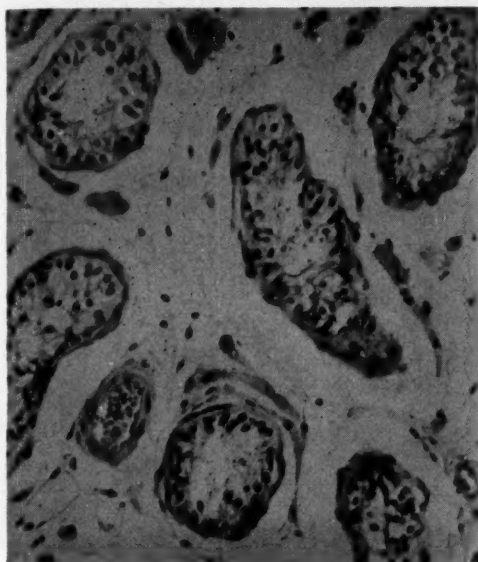
Fig. 1.—Photomicrograph of a representative portion of one of the testes of Case 2.

Treatment.—Postcastrational flushes were not reported. Oral, cyclic estrogen therapy was started 2 months after operation and after a year only a minimal increase in breast development occurred.

CASE 3.—The sex of this patient, aged 14 years, 10 months, had been certified as female and the patient had been reared accordingly. At pubescence, occurring between 12 and 13 years of age, a low-pitched voice and some facial hirsutism had developed. There were a hypoplastic phallus with hypospadias and chordee, a bifid empty scrotum, a rudimentary vaginal pouch, bilateral inguinal gonads, and slight gynecomastia (Figs. 2 and 3).

Urinary Hormones.—Preoperative values were urinary gonadotropins 20. R. U. U. per 24 hours (5 times average normal) and urinary 17-ketosteroids 15.7 mg. per 24 hours (normal).

Operative Findings.—Exploratory laparotomy showed no pelvic female organs. The inguinal gonads and the epididymides were removed.

Histopathology of Testes.—The architecture was essentially normal save for some clumping of normal-appearing Leydig cells. The tubules were of normal size and contained only Sertoli cells and occasionally some spermatogonia. There were slight hyalinization and fibrosis of the tubules.

Treatment.—Postcastrational flushing was controlled promptly by oral cyclic estrogen therapy. Breast development progressed to the adult stage.

CASE 4.—The sex of this patient, aged 15 years, had been certified as female and the patient had been reared accordingly. There were a hypoplastic phallus with hypospadias, a bifid empty scrotum, a rudimentary vaginal pouch, bilateral inguinal gonads, and slight gynceomastia.

Fig. 2.—Left, Case 3 prior to treatment. Right, the patient four months after castration and during estrogen therapy.

Urinary Hormones.—Preoperative values were urinary gonadotropins 25 R. U. U. per 24 hours (6.25 times average normal) and urinary 17-ketosteroids 27.2 mg. per 24 hours (slightly increased). Values during initiation of estrogen therapy were urinary gonadotropins 20 R. U. U. per 24 hours (5 times average normal) and urinary 17-ketosteroids 11.55 mg. per 24 hours (normal). Values following cessation of estrogen therapy for 2 weeks were urinary gonadotropins 12 R. U. U. per 24 hours (3 times average normal) and urinary 17-ketosteroids 11.32 mg. per 24 hours (normal). Values after estrogen therapy had been stopped for 30 days were urinary gonadotropins 30 R. U. U. per 24 hours (7.5 times average normal) and urinary 17-ketosteroids 8.38 mg. per 24 hours (slightly low).

Operative Findings.—Exploratory laparotomy showed no pelvic female organs. The inguinal gonads and their nonunited epididymides were removed.

Histopathology of Testes.—The tubules were of normal size and number, but they were completely hyalinized with peritubular fibrosis. They contained only Sertoli cells save for a few germinal cells which were presumably spermatogonia. Leydig cells appeared to be increased in number and were condensed in sheets and clumps.

Treatment.—Postcastrational flushing was controlled promptly by oral cyclic estrogen therapy. Continuation of estrogen therapy resulted in breast development to the adult stage, redistribution of weight and development of a gynecoid hair pattern. The psychosexual response was adequately gynecoid. A well-developed vagina resulted from coitus. There was shrinkage of the phallus.
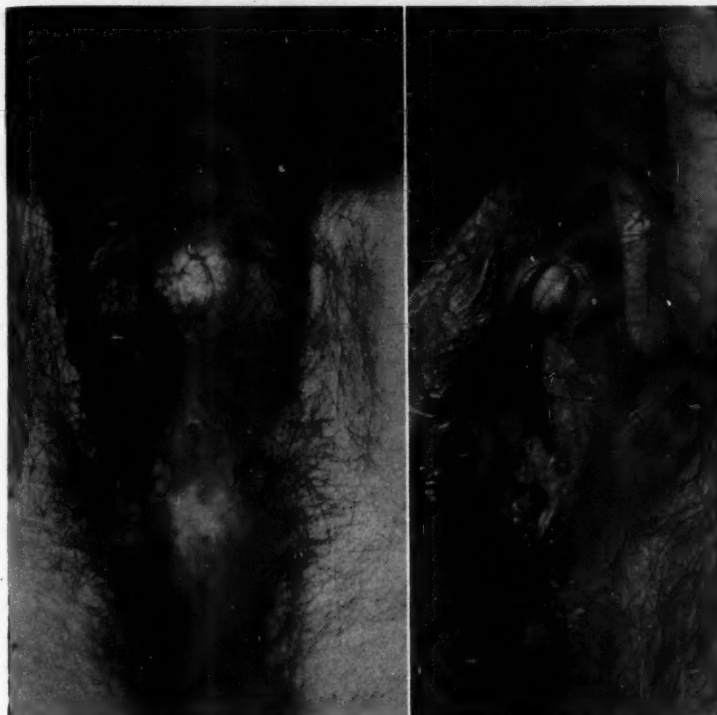
Fig. 3.—Left, perineum of Case 3, prior to treatment. Right, shrinkage of phallus following castration and four months of estrogen therapy.

CASE 5.—The sex of this patient, aged 16 years, had been certified as female and the patient had been reared accordingly. A hypertrophied "clitoris" had been amputated at the age of 3 years. There were an erectile phallic stump with hypospadias, an empty rugated labioscrotum, a rudimentary vaginal pouch, and slight gynecomastia. Facial hirsutism, and a husky voice had developed since pubescence (Figs. 4 and 5).

Urinary Hormones.—Preoperative values were urinary gonadotropins 35 R. U. U. per 24 hours (8.75 times average normal) and urinary 17-ketosteroids 3.6 mg. per 24 hours (approximately one-third low range of normal). Values during estrogen therapy were urinary gonadotropins less than 2 R. U. U. per 24 hours (low) and urinary 17-ketosteroids 1.8 mg. per 24 hours (markedly low). Values after estrogen therapy had been stopped for 4 months were urinary gonadotropins 30 R. U. U. per 24 hours (7.5 times average normal) and urinary 17-ketosteroids 2.9 mg. per 24 hours (moderately low).

Operative Findings.—Exploratory laparotomy showed a small uterus, approximately 1 cm. in greatest dimension. Only one gonad, a testis with no Wolffian appendages, was found. Its location was pelvic. There were 2 "tubes" attached to the uterus. The testis, most of the uterus, and the "tubes" were removed.

Histopathology of Testis.—The tubules were of normal size and number but they were completely hyalinized with peritubular fibrosis. They contained only Sertoli cells. There were striking condensation and apparent hyperplasia of normal-appearing Leydig cells (Fig. 6).

Other Histopathology.—One of the presumed "tubes" was identified as a Wolffian structure. The endometrium contained moderate numbers of glands with resting cells (Fig. 7).

Treatment.—There was no postcastrational flushing. Oral cyclic estrogen therapy yielded gynecoid responses, including development of breasts to adult stage, enlargement of uterus and cervix, and regular withdrawal bleeding. Estrogen therapy was stopped for 14 months during which time there were 4 episodes of scanty bleeding after irregular intervals. There were no genital regression and no flushing.
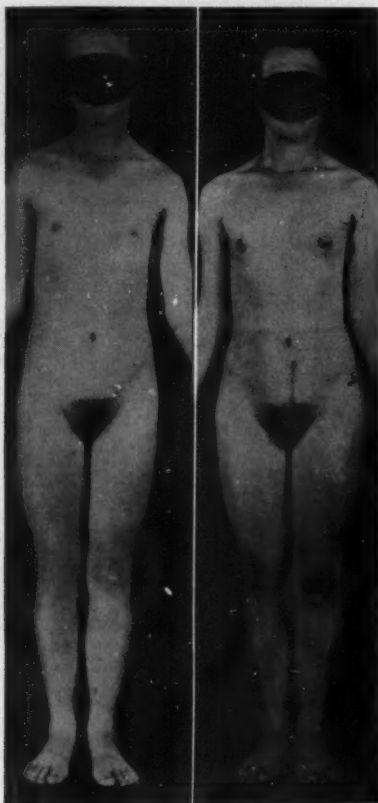
Fig. 4.—Left, Case 5 prior to treatment. Right, patient after castration and a year of estrogen therapy.

CASE 6.—The sex of this patient, aged 17 years, had been certified as male and the patient had been reared accordingly. Pubescence began at 12 years of age and there had occurred erections and seminal emissions. There were a normal-sized penis with hypospadias, an empty, small, but not bifid scrotum and a somewhat gynecoid habitus. There was no gynecomastia.

Seminal Findings.—Azoospermia.

Operative Findings.—Exploratory laparotomy showed no pelvic female organs. Both testes with their appendages were in pelvic location. Biopsy and orchidopexy were done on the left side.

Histopathology of the Testis.—The tubules were of normal size and number but they were hyalinized with slight fibrosis. They contained essentially Sertoli cells, although a few presumed spermatogonia were seen. There was slight clumping of apparently normal and slightly increased Leydig cells.

Treatment.—None save the surgery.

CASE 7.—The sex of this patient, aged 17 years, 9 months, had been certified as male and the patient had been reared accordingly. There were a normal-sized penis and an empty well-developed scrotum. There was no hypospadias or gynecomastia.

Fig. 5.—Perineum of Case 5 prior to treatment.
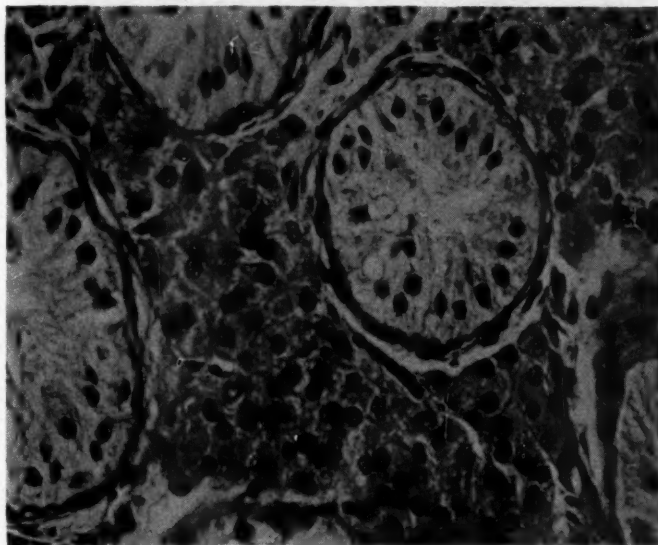
Fig. 6.—Photomicrograph of a representative portion of the testis of Case 5.

Seminal Findings.—Azoospermia.

Urinary Hormones.—Preoperative values were urinary gonadotropins 30 R. U. U. per 24 hours (7.5 times average normal) and urinary 17-ketosteroids 3.6 mg. per 24 hours (moderately low).

Operative Findings.—Exploratory laparotomy for acute abdominal pain showed a small uterus, cervix, 2 tubes, and a vagina. The left testis lay at the opening of the inguinal canal
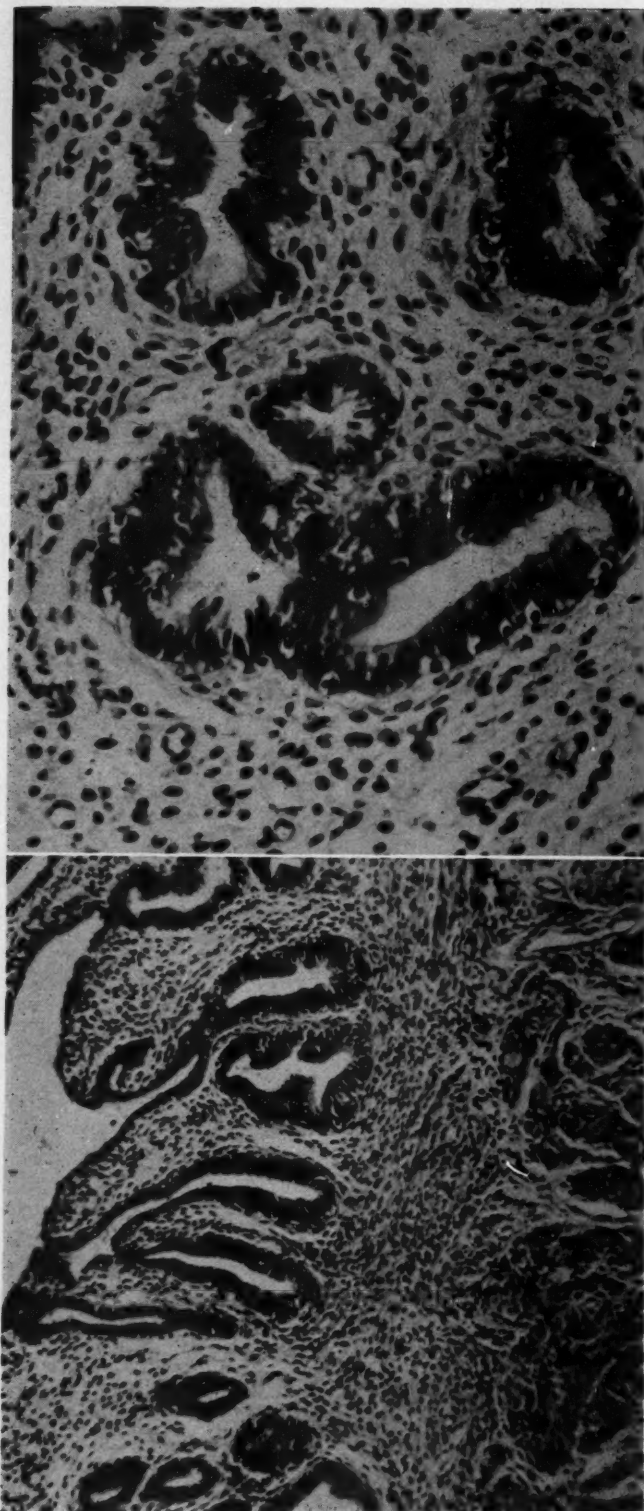
Fig. 7.—Low and high power photomicrographs of the endometrium of Case 5.
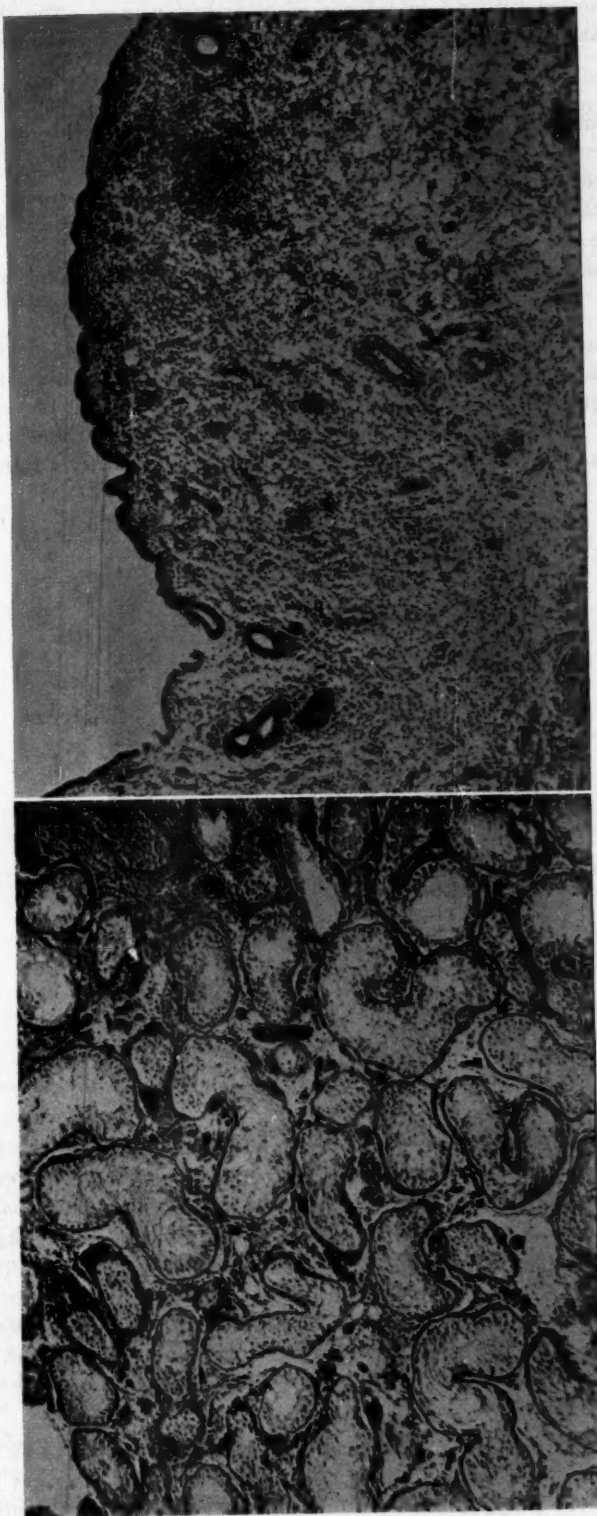
Fig. 8.—Left, photomicrograph of the left testis of Case 7. Right, photomicrograph of the endometrium of Case 7.

and it was not connected with an epididymis or other appendages. The right testis was of abdominal location and was necrotic due to torsion. The gonads and the pelvic female structures were removed.

Histopathology of Testes.—The tubules were of normal size and number but there were marked thickening of the basement membranes and hyalinization. They contained essentially Sertoli cells with very occasional presumed spermatogonia. The Leydig cells were of normal appearance and number (Fig. 8).

Other Histopathology.—The endometrium contained moderate numbers of glands with resting cells (Fig. 8).

Treatment.—Surgery only. The patient died 1 month after operation from intestinal obstruction.

CASE 8.—The sex of this patient, aged 18 years, had been certified as female and the patient had been reared accordingly. Bilateral swellings in the inguinal regions had been present since the age of 7 years. Pubescence began at the age of 13 years and resulted in female breasts of adult type but no genital bleeding occurred. There were a hypoplastic phallus with hypospadias, an empty bifid scrotum, and a rudimentary vaginal pouch.

Fig. 9.—Photomicrograph of a representative portion of one of the testes of Case 8.

Operative Findings.—Exploratory laparotomy showed no pelvic female organs. The inguinal masses were identified as testes with their appendages. These were removed.

Histopathology of Testes.—The tubules were of normal size and number, with slight fibrosis and hyalinization. They contained essentially Sertoli cells, although a few presumed spermatogonia were seen. There was moderate clumping of apparently normal but moderately increased Leydig cells (Fig. 9).

Treatment.—There was severe postcastrational flushing for 3 to 6 months following surgery, 12 years ago. There was no estrogen therapy. The patient was married at the age of 19 years and one year later reported normal and satisfactory coital activity. There has been no further follow-up.

CASE 9.—The sex of this patient, aged 23 years, had been certified as female and the patient had been reared accordingly. There had been swelling in the right inguinal region for 2 years. There were a hypoplastic phallus with hypospadias, an empty labioscrotum, a vaginal pouch 2.5 cm. in depth, and gynceomastia comparable to adult female breasts (Fig. 10).

Operative Findings.—Exploratory laparotomy showed no pelvic female organs. Grossly normal testes with appendages lay in the upper portion of the inguinal canals. These were removed and the phallus was amputated.

Histopathology of Testes.—The tubules were of normal size but apparently decreased in number. There were marked hyalinization and striking fibrosis. The tubules contained preponderantly Sertoli cells with a few presumed spermatogonia. There was marked clumping and apparent increase of normal-appearing Leydig cells (Fig. 11).

Treatment.—Surgical only. There has been no follow-up during the ten years which have elapsed since operation.

Fig. 10.—Case 9 prior to treatment.

CASE 10.—The sex of this patient, aged 27 years, had been certified as female and the patient had been reared accordingly. Pubescence began at the age of 16 years. Since that time there has been progressive hirsutism. Bilateral inguinal swellings had been observed for 12 years. There were a hypoplastic phallus with hypospadias, the urethral opening being located within a vaginal pouch which was 2 inches in depth, an empty bifid scrotum, and gynecomastia comparable to adult female breasts.

Operative Findings.—Exploratory laparotomy showed no pelvic female organs. The inguinal masses were identified as testes with their appendages. These were biopsied and left in situ.

Histopathology of Testes.—The tubules were essentially of normal size but were reduced in number. There was moderate hyalinization and fibrosis. The tubules contained essentially Sertoli cells but there were some presumed spermatogonia and primary spermatocytes. There were marked condensation and increase of normal-appearing Leydig cells.

Treatment.—Surgery only. There has been no follow-up.

CASE 11.—The sex of this patient, aged 26 years, had been certified as female and the patient had been reared accordingly until study and treatment at the age of 13 years. Pubescence had not occurred then and the findings included a small phallus with chordee and hypospadias, a bifid scrotum, a normal-sized right scrotal gonad, an inguinal left gonad, and no gynecomastia.

Seminal Findings.—No examination at the age of 13 years. At the age of 26 years, azoospermia.

Urinary Hormones.—These were not studied at the age of 13 years. The values at the age of 26 years were urinary gonadotropins 9 R. U. U. per 24 hours (2.25 times average normal) and urinary 17-ketosteroids 13.42 mg. per 24 hours (normal).
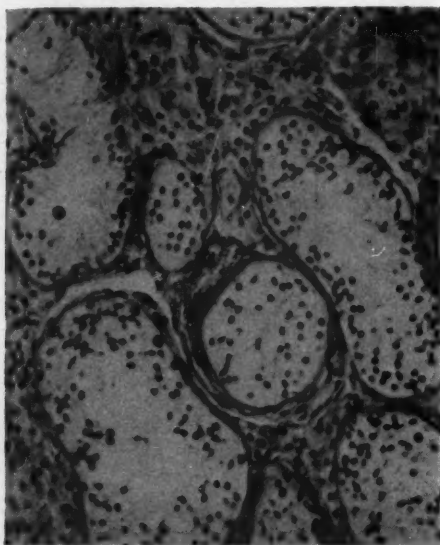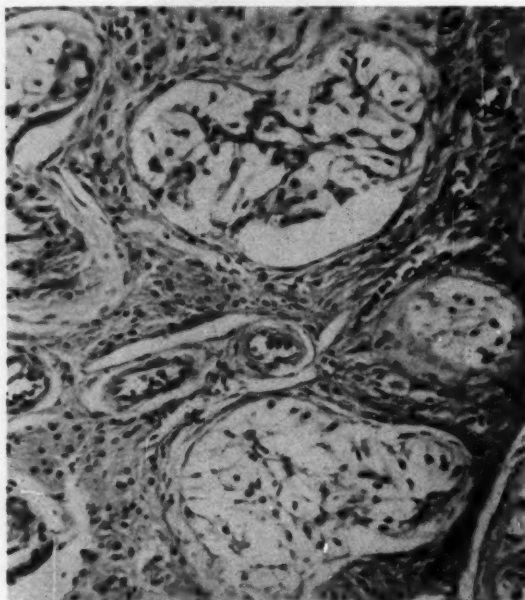

Fig. 11.—Photomicrograph of a representative portion of one of the testes of Case 9.

Operative Findings.—Exploratory laparotomy at the age of 13 years showed no pelvic female organs. The gonads were not biopsied.

Treatment.—Following the laparotomy, it was decided that the patient should be a male. Therapy with chorionic gonadotropins and testosterone propionate was given preparatory for plastic surgery of the urethra. The left inguinal gonad did not descend under this therapy, although pubescence occurred. Gynecomastia developed, although there were some android responses. A number of unsuccessful urological operations for hypospadias were done. A left orchidopexy was done at the age of 18 years. The present status of this patient, who was surveyed recently by the endocrinological staff, is that of a socially maladjusted, sexually frustrated individual with a record of a number of petty encounters with the police. The patient was married, as a male, at the age of 21 years and was divorced 4 years later, following a questioning in court of the patient's sexual status. At present there are breasts of adult gynecoid type, android muscularity, a phallus of small size, and relatively small scrotal gonads. At present, the patient is under neuropsychiatric care. Because of the neuropsychiatric status, biopsies of the testes have not yet been done.

Analysis and Discussion of Clinical Data

Some of the clinical data which are pertinent to this restricted study are analyzed and discussed.

Distribution of Patients and Methods of Study.—The 11 patients ranged in age from 4 years, 9 months to 27 years. Three had Müllerian derivatives, whereas 8 were lacking in these.

Six of these patients had determinations of urinary gonadotropins and 17-ketosteroids and 5 of the 6 had histopathological studies of the testes. Five had only histopathological studies. The 6 patients who had full endocrinological investigation and whose handling was directed by the endocrinological staff had thorough neuropsychiatric investigation with particular reference to the android or gynecoid orientation.

The urinary gonadotropins and 17-ketosteroids were determined by methods developed by A. A. Salmon in the laboratory of the Division of Endocrinology. The urines of these patients were quantified by A. A. Salmon, Ruth Weisner, and Betty Henry. The range of urinary gonadotropins for normal adult females, exclusively of ovulatory peaks, for this method is 2 to 10 R. U. U. per 24 hours, the average normal being 5 R. U. U. The range for normal adult males is 2 to 8 R. U. U. per 24 hours, the average normal being 4 R. U. U. The range of urinary 17-ketosteroids for normal adult females for this method is 4 to 14 mg. per 24 hours. The range for normal adult males is 10 to 22 mg. per 24 hours. The values of urinary gonadotropins and 17-ketosteroids of the patients of this study have been interpreted in terms of range and average for normal adult males.

The specimens of testes were studied histopathologically by members of the pathology staff and by two of us (E. C. H. and J. Z.). The descriptions of histopathology are ours but these do not disagree materially with those reported by the pathologists.

Testes of Male Pseudohermaphroditism.—Their location may be abdominal, inguinal, labioscrotal, or scrotal. When the testis has abdominal location, the epididymis and vas may be unconnected and may be in inguinal or scrotal location.[7] In general, the testes of male pseudohermaphroditism tend to be smaller than normal scrotal testes.

Even prior to pubescence, cryptorchid testes may show abnormalities other than that of location. A fibrosing tendency has been described as early as the fourth year of age.[8]

Characteristic degenerative changes occur at the time of pubescence. These may be related etiologically to inherent genetic abnormalities, the thermal differential of the abnormal location, and to the upswing in the gonadotropic activity of the pituitary, responsible for pubescence.[9] Accordingly, the histopathological characteristics of these testes depend upon the age of the patient, upon the status of pubescence, and upon their location. In general, post-pubescent testes in low inguinal or high scrotal location show less degeneration than those in abdominal position.

There are, however, patients with scrotal small testes in whom essentially the same gonadal histopathology is found as in patients with abdominal testes. These patients conform to the syndrome of Klinefelter, Reifenstein, and Albright.[10] To emphasize the similarity of the patients of the Klinefelter, Reifenstein, and Albright syndrome and those with cryptorchidism, we have referred to the former as "scrotal cryptorchids."[9]

The specific degeneration which characterizes the testes of male pseudohermaphroditism and of cryptorchidism in general concerns the seminiferous tubules. Cytologically the germinal epithelium is affected most, but the supporting or Sertoli cells, although they may appear normal, are altered in their functional capacities, as subsequent discussion will indicate. The degeneration of the germinal epithelium is progressive and, when complete, results in total destruction and hyalinization. There is usually marked tubular fibrosis. The

tubules are usually normal in caliber and number, a fact which indicates that ample testosterone is being supplied by the Leydig cells for their growth and maintenance. The tubules may be collapsed, however, by the marked condensation and hyperplasia of the Leydig cells. This hyperplasia can be related to the hypergonadotropic action of the pituitary, sequential to degeneration of the tubules. Although the Leydig cells involved in this condensation and hyperplasia appear normal, these patients commonly are hypoandrogenic. As some of our group[11] have shown for patients with other testicular abnormalities, there are no correlations between the number of apparently normal Leydig cells, the urinary 17-ketosteroids, and the degree of androgenism of these patients.

Hypergonadotropuria.—This does not develop in male pseudohermaphroditism or in the patients of the syndrome of Klinefelter, Reifenstein, and Albright until pubescence. It is caused by the degenerative changes of the seminiferous tubules which result in a failure of release of an inhibiting hormone, believed to be estrogen. The degree of hypergonadotropuria is proportional to the degeneration of the tubules. The hypergonadotropuria may be comparable to that which occurs in castrated males and females. The hypergonadotropuria involves chiefly the follicle-stimulating gonadotropin (F. S. H.) which normally monitors spermatogenesis.

In our 6 patients hypergonadotropuria ranged from 2.25 times to 8.75 times average normal. Case 2, aged 14 years, had a hypergonadotropuria of 3 times with primary spermatocytes, spermatogonia, and Sertoli cells in the seminiferous epithelium. (We would prognosticate that a few years later the hypergonadotropuria and the degeneration of the seminiferous tubules would have been much more marked.) Four other patients (Cases 3, 4, 5, and 7), whose ages ranged from 14 years, 10 months to 17 years, 9 months, had hypergonadotropuria which ranged from 5 times to 8.75 times. The seminiferous epithelium of these patients contained only Sertoli cells or Sertoli cells and occasional spermatogonia. Case 11, aged 26 years, with hypergonadotropuria of 2.25 times, had scrotal testes and azoospermia. The azoospermia, in the absence of histopathological studies, has been related tentatively to ductular blockage, because of the thickened epididymides and beaded vasa of the patient. The scrotal location of the testes of this patient would tend to minimize degeneration of the seminiferous tubules and the degree of hypergonadotropuria.[9]

Mechanism of Hypergonadotropuria.—As we have observed, degeneration of the seminiferous epithelium results in impaired release of an inhibiting hormone which monitors the secretion of the follicle-stimulating gonadotropin (F. S. H.) by the pituitary. We accept the generally current belief that this inhibiting hormone is estrogen and that it is secreted by the Sertoli cells, which are homologues of granulosa cells of the ovary. This hypergonadotropuria occurs despite hyperplasia of apparently normal-appearing Leydig cells, which are the homologues of the theca cells of the ovary. Although the secretion of androgen by these hyperplastic Leydig cells may not be normal, these patients afford ample clinical evidence that androgen is secreted by these cells. The occurrence of hypergonadotropuria under these circumstances emphasizes that the prime hormone in monitoring the intensity of gonadotropic action is not androgen but is the inhibitory hormone of the seminiferous epithelium, namely, estrogen.

The evidence in favor of estrogen secretion by the Sertoli cells includes the following:

1. The existence of estrogen-producing Sertoli-cell tumors of the testes of dogs has been established.[12] Teilum[13] has described an estrogen-producing Sertoli-cell tumor of the testis in man.

2. Estrogen therapy promptly reduces hypergonadotropuria in males, whereas full substitution doses of testosterone propionate produce relatively slight decreases in this hypergonadotropuria.

3. In true hermaphroditism, in which there are ovarian and testicular elements, the urinary gonadotropins are essentially normal,[14] even in patients in whom the cryptorchid testis moiety has undergone typical degeneration of the seminiferous tubules. The normal urinary gonadotropins of these patients are due to the secretion of estrogen by the ovarian moiety. We have made a differential diagnosis between female pseudohermaphroditism and male pseudohermaphroditism in a postpubescent patient with essentially normal urinary gonadotropins and urinary 17-ketosteroids which were twice normal.

4. The relation of estrogen secretion to the Sertoli cells is more logical embryologically than its relation to germ cells, which are the homologues of the primary sex cells. The relation of estrogen secretion to the germ cells would be comparable to relating estrogen secretion in the female to the ova.

The assumption that the elaboration of estrogen by the Sertoli cells of these patients with hypergonadotropuria is impaired, despite their persistence and apparent cytologic normalness, is not an inconsistent one. It is held that the degenerative changes within the seminiferous tubules are caused by impairment of the tubular blood supply and that, as the degeneration progresses and the fibrosis and thickening of the lamina propria increase, the blood supply is further impaired. The germinal cells, being arranged in layers, are more susceptible to this blood impairment than the Sertoli cells and, accordingly, the disruption of the germ cells is more striking from a cytological point of view. The Sertoli cells, however, are impaired in their function, despite the fact that, by ordinary staining methods, they appear to be intact. Histochemical staining methods at present do not permit a gauging of steroid secretion by cells of the gonads or of the adrenal cortex.[11]

Urinary 17-Ketosteroids.—Urinary 17-ketosteroids in the male are derived from the metabolism of adrenal and testis androgens. Since they are measured colorimetrically and since some 17-ketosteroids are of low or no androgenicity, values for these steroids do not reflect necessarily the androgenicity of the individual. Biological estimations of urinary androgens are required for this purpose. The qualitative partitioning of various urinary 17-ketosteroids, androgenic and relatively nonandrogenic ones, is doubtlessly different for normal males and for male pseudohermaphrodites. It is possible, therefore, that the values for urinary 17-ketosteroids may be increased in some patients with male pseudohermaphroditism and yet there may be relatively low androgenicity.

The range of preoperative values of urinary 17-ketosteroids of our patients was 3.6 mg. per 24 hours (approximately one-third low range of normal) to 27.2 mg. per 24 hours (slightly increased). There were no correlations between hyperplasia of Leydig cells, values for urinary 17-ketosteroids, degree of hypergonadotropuria and android or gynecoid psychosexual patterns. Marked gynecomastia occurred in patients with low, normal, and increased urinary 17-ketosteroids. Castration commonly reduced urinary 17-ketosteroids by amounts which varied from 20 to 60 per cent. Estrogen therapy tended to reduce less strikingly urinary 17-ketosteroids.

Gynecomastia.—Gynecomastia was present in 6 of 11 patients, prior to any estrogen therapy. In one of these 6 patients, gynecomastia was related to therapy with chorionic gonadotropins and testosterone propionate at the age of 13 years and before pubescence. The gynecomastia appears uniformly as a manifestation of pubescence, unless there has been antecedent steroid or gonadotropic therapy. The degree of gynceomastia ranged from that comparable to

the "bud stage" of female adolescence in 3 patients to that comparable to adult female mammary development in 3 patients. The degree of hypergonadotropuria bore no relationship to the presence of gynecomastia. The cause of gynecomastia of these patients is not known but seems most likely related to an abnormal steroid metabolism, which doubtlessly involves the adrenal cortex. It is not due to relative or absolute increases in estrogens, which are incompatible with the hypergonadotropuria and the predicated impaired secretion of estrogens by the Sertoli cells. The histopathology of this gynecomastia is quite different from that which is produced in males by estrogen therapy.[10] There is an additional etiological possibility, namely, that a genetic abnormality intrinsic to the breasts may exist, which predisposes them to stimulation by an abnormal steroid homeostasis.[9]

Endometrium.—Endometria of 2 patients were studied. Although these were relatively hypoplastic and contained glands with cells of low activity, they were surprisingly well proliferated considering the fact that they were monitored by testes rather than by ovaries. Incidentally, the patient with the most striking hypergonadotropuria (8.75 times), representative of the least estrogen secretion, had the best proliferated endometrium. Subsequently, these endometria responded typically to estrogen therapy. The small remnant of uterus which was left when Case 5 was operated upon showed a surprising degree of hyperplasia and development during estrogen therapy.

The Gonads and the Psychosexual pattern.—Eight of 10 patients, omitting the patient who was aged 4 years and 9 months, were certified as females, had been reared accordingly, and were acceptably oriented as females. One of these patients had a scrotal testis. Accordingly, these patients point up the fact that sexual orientation and psychosexual behaviorism are not prime functions of the gonads.[15] Generally speaking, a male pseudohermaphrodite accepts the sex which is certified and assigned.

A consideration of the accepted and manifested psychosexual pattern of male pseudohermaphroditism is paramount to success in treatment. Neuropsychiatrists render invaluable assistance in assessing the android-gynecoid ratio of these patients. The psychosexual failure of Case 11 can be related to ignoring the accepted and manifested psychosexual pattern of the patient.

Castration.—We believe that castration constitutes an important phase of the furthering of gynecoid orientation and development of male pseudohermaphrodites with this sexual trend. Some of the considerations which appear to justify castration are:

1. Participation of the testes in abnormal steroid metabolism is avoided.
2. Estrogenization is facilitated.
3. Neoplasia of cryptorchid testes is avoided.
4. The patient feels more secure, knowing that the undesired male gonads have been removed.

Flushing commonly followed castration of these patients. The fact that these patients had hypergonadotropuria, comparable in some instances to that of climacteric females, and the fact that this hypergonadotropuria has been related to decreased estrogen secretion by the Sertoli cells, indicate that postcastrational flushing of these patients did not result simply from subsequent hypergonadotropuria or from estrogen withdrawal. The flushing, however, was promptly relieved by estrogen therapy. Obviously, the postcastrational flushing of these patients and the flushing which follows castration of normal females involve entirely different preoperative patterns of homeostasis, despite the fact that postoperatively labile phases of compensation leading to ultimate endocrine homeostasis may be similar in both groups of individuals.[16]

Following castration, the levels of urinary gonadotropin may exceed the preoperative ones. This may indicate that the testes, either by some residual estrogen secretion or by their androgen secretion, have exerted some inhibiting effects on the pituitary. The postcastrational hypergonadotropuria is reduced and brought to normal levels by estrogen therapy and recurs when estrogen therapy is discontinued.

Effects of Estrogen Therapy.—For the estrogenization of patients with gynecoid orientation, we have employed a preparation of conjugated estrogens (Premarin) which was given orally. The schedule of the usual cyclic therapy is 3.75 mg. daily for 20 days and withdrawal, of treatment for 10 days.

Estrogen therapy in male pseudohermaphroditism produces similar responses to those of apubescent or hypopubescent females, subject, of course, to the limitations imposed when female internal genital organs are absent. These responses occur in both castrated and noncastrated individuals. Castration facilitates the responses and doubtlessly is responsible to a great degree for those related to deandrogenization.

Some of the beneficial alterations which characterize estrogenization are:

1. Breast development occurs, even when no antecedent gynecomastia existed.

2. There results a redistribution of fat according to a gynecoid pattern.

3. General and facial hirsutism is reduced.

4. There is alteration of the android pubic hair pattern to one of gynecoid type.

5. The phallus ceases to be erectile and usually decreases in size.

Postpubescent castration and estrogenization do not alter the lowered android pitch of the voice.

As we have previously observed, estrogen therapy may produce marked growth and development of hypoplastic uteri and, when the therapy is given cyclically, regular withdrawal bleeding may result. The continuation of episodes of bleeding for 14 months, after the discontinuation of estrogen therapy, as reported by Case 5, cannot be explained. We have been assured that during this time the patient has not received estrogen therapy. Laparotomy revealed only 1 gonad but one of us (F. B. C.) was unable, despite a careful search, to locate another gonad. That the patient should have a remaining ovary appears inconsistent with the hypergonadotropuria and its response to estrogen therapy. Unfortunately, we have not had an opportunity to examine this patient during these 14 months and we believe that, had this been done, the cause would have been ascertained.

Sociological and Medicolegal Aspects.—These are numerous. One of the questions which these patients pose is, what is their rightful sex? Is it the sex certified by the obstetrician at birth, or is it the sex which corresponds to the male gonads, or is it the sex accepted by the individual and manifested by the individual's psychosexual pattern? It is our belief that from the standpoint of psychological expediency and clinical practicality the correct sex is that which the individual desires and to which there is orientation. This sex usually conforms to that certified at birth. Neuropsychiatric assistance should be sought in determining the sexual orientation of these patients. Furthermore, there should be a full understanding on the part of the patient and the parents of what is planned and what can be done, with due consideration of all limitations. When gonadectomy is planned, adequate permission should be obtained.

Complications may arise when it seems necessary to alter sex from that certified by birth registration. The frequent needs which now arise for copies of birth certificates may create a psychological and social crisis for such an indi-

vidual. Under these circumstances, the birth certificate should be altered to indicate the new sex. We are not sure about the legality of this or other aspects of male pseudohermaphroditism. We regard the medicolegal aspects of male pseudohermaphroditism as worthy of study.

These patients also pose a question as to what is the correct meaning of homosexuality. Male pseudohermaphrodites with gynecoid orientation are by definition homosexual. We may inquire what is the difference between these patients and homosexual males with scrotal testes? Are male pseudohermaphrodites homosexuals after they have ·been castrated and estrogenized? Under these circumstances, what is their sociological sex and their medicolegal sex? For instance, one of our patients, following castration and without estrogen therapy, married as a female and reported normal coital activity and connubial adjustment. What would be the legal status of this marriage, if evidence was submitted that the patient was a castrated male, despite certification at birth as a female? Another of our patients, following castration and estrogenization, has developed an active sexual drive with gynecoid orientation and has been practicing satisfactory coitus with an apparently normal male. Should this patient marry, provided the proposed husband knows that menstruation and childbearing are impossible? These are a few of the sociological and medicolegal questions which these patients pose to us. We hope to find the answers.

Summary

Studies of eleven male pseudohermaphrodites from the standpoint of histopathology of the testes, levels of urinary gonadotropins and 17-ketosteroids, and psychosexual orientation have been reported. Particular attention has been paid to those patients with gynecoid psychosexual patterns. The results of castration and estrogenization of these patients have been discussed. Responses of local target organs to estrogen therapy have been considered. Justification for castration of these individuals is presented. The beneficial effects of estrogenization have been discussed. Some of the sociological and medicolegal questions posed by these patients have been considered.

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Discussion

DR. OREN MOORE, Charlotte, N. C.—This paper presents an unusually large number of this type of unfortunate individuals, individuals on whom nature has played one of its

most ghastly tricks, individuals whose status socially, legally, and sexually has been undetermined except by the most superficial criteria and whose status is most often decided on the flimsy evidence available at the time of birth, evidence which is often determined by unskilled observers and whims of disappointed parents.

Dr. Hamblen and his associates through the technique of endocrine evaluation attempt to show that it is possible to arrive at a more or less accurate scientific conclusion as to the sex to which these unfortunates really belong, and then to proceed by surgery and by therapy to accent the characteristics both physical and physiological to a degree which may permit them to assume a definite status in life.

Such methods of determination as are expressed in this paper are not of course available to the average clinician, and it is most fortunate for both doctor and patient that institutions and specialists of the high grade that is exemplified by Dr. Hamblen and Duke University are available for consultation and treatment.

In the past, pseudohermaphroditism has produced some most startling transformations of individuals from one sex to another, but in almost every instance the procedure which brought about such transformation was accidental or freakish to a degree, and certainly not the result of a planned campaign. One has only to remember the startling and almost comic history of Vivian Leigh who, competing as a member of the American Woman's Olympic Track Team in the 1939 Olympic meet, simply swept the field, winning the total of some 60 points for her American co-contenders and being crowned as perhaps the world's greatest woman athlete; only to have upon her return to America the startling discovery that she was not a woman but a man, and, of course, she had to give up all claims for feminine championships. The history of medicine is replete with more or less humorous stories of such accidental changing of sex, in most instances brought about by attempts at plastic surgery, with no concept on the part of the operator of the enormous sociologic and therapeutic implications.

I cannot, of course, speak with personal knowledge of the technique of endocrine diagnosis which the essayists have employed, but I have been priviledged from time to time to take part in some of the surgical cures of these anomalies and I know in some measure the immense sense of gratitude that is displayed by these victims of Nature's grim pranks.

THE ROLE OF MARGINAL SINUS RUPTURE IN ANTENATAL HEMORRHAGE*

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CESAREAN section undertaken for painless hemorrhage with a presumptive diagnosis of placenta previa frequently discloses a normally situated placenta. Likewise, the vaginally delivered placentas in cases of hemorrhage often reveal, on examination, no evidence of low implantation. In addition, many studies of bleeding in late pregnancy and labor include a high percentage of cases for which no demonstrable cause is found.

As a possible explanation for these facts, close examination of the placenta has shown, in our experience, that rupture of the placental blood channel known as the marginal sinus is responsible for many hemorrhages mistakenly ascribed to placenta previa or to abruptio placentae or causes unknown.

Knowledge concerning the existence of and possible clinical conditions referable to the marginal sinus has existed for more than a century. Jacquemier, in 1839, Duncan, in 1875, Budin, in 1893 and 1896, wrote concerning it. Jellett (Dublin) included the torn sinus as a source of hemorrhage in placenta previa. In the American literature, there is little discussion of rupture of the marginal sinus. Eastman emphasizes the likelihood of confusing it with abruptio placentae. De Lee considered it to be a rare cause of bleeding. Other authors either fail to allude to it or do not associate it with abnormal bleeding.

Anatomy and Function of the Marginal Sinus; Susceptibility to Injury

The marginal sinus is a constant peripheral placental structure situated just outside or just within the marginal cotyledons beneath the Waldeyer ring, composed for the most part of a thin velamentous wall closely approximated to the reflection of the membranes from the placental margin, but sometimes involved in the fibrous chorionic and decidual degenerative concentrations at this site. These cause variation in the caliber of the sinus and the thickness of its wall, as well as in its elasticity and resistance. The luminal diameter varies between five millimeters and two centimeters.[1]

Functionally, the sinus is intermediate between the subchorionic and intercotyledonary maternal blood spaces of the placenta and the large venous sinuses of the uterus which are concentrated beneath the marginal zone, thus constituting a link in the return blood flow from the placental bed to the uterine circulation. Ostia on the medial sinus wall providing communication with the subchorionic space are readily visible, while the major uterine communications are disrupted by the uteroplacental plane of separation. Rents, therefore, in the sinus wall of the delivered placenta are to be expected and are not, of themselves, indicative of antenatal rupture.

As one examines the marginal sinus in the placenta of advanced pregnancy, he is impressed with the fragility of its transparent membranous wall, as well as a greater vulnerability due to its location, with little or no peripheral support; also, that it may be subject to stresses placed upon the membranes at their placental attachment.

It is understandable why the marginal sinus, under stress, may fail to contain the volume of maternal blood reaching the periphery. It is likewise understandable why its rupture may be compatible with the continuation of pregnancy since, with cessation of hemorrhage, the placenta remains healthy and its implantation still secure. Small valvelike flaps at the medial sinus wall fenestrations may offer, in addition to thrombosis, explanation for spontaneous cessation of placental marginal hemorrhages.
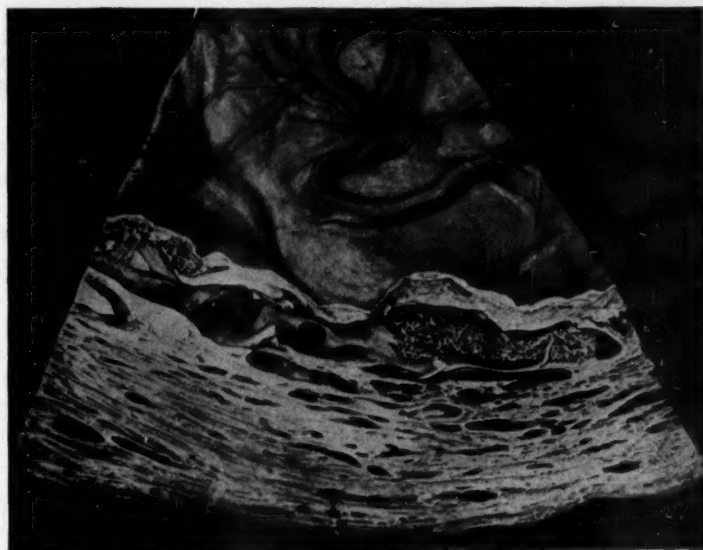
Fig. 1.—Tangential section of in situ placenta at margin, showing medial and inferior wall fenestration in marginal sinus, establishing communication with intercotyledonary spaces and uterine sinuses. Villous tufts visible. (From Spanner.[1])

Clinical Behavior and Diagnostic Features

In consideration of hemorrhage from the marginal sinus of the normally implanted placenta, we have thought it instructive to draw various comparisons with that from placenta previa and abruptio, the major causes of hemorrhage of advanced pregnancy and labor. Observations were made upon 147 cases of hemorrhage of the third trimester or of labor when of such an amount as to be of concern to the attendant.* These occurred among 2,655 consecutively delivered gravidas, each attended personally by one of our group. The distribution of causes of hemorrhage in this series is indicated in Table I.

Vaginal examination, when indicated and informative, and study of the placenta furnished the most reliable information in classifying these cases as placenta previa, abruptio, or rupture of the marginal sinus and these examinations have been given prior consideration.

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*Abstracts of 50 cases of marginal sinus rupture available in authors' reprints.

TABLE I. CAUSES OF HEMORRHAGE, LATE PREGNANCY AND LABOR (147 CASES)

	NUMBER	PER CENT
Placenta previa (17 proved)	51	34.6
Ruptured marginal sinus	50	33.9
Abruptio placentae	14	9.6
Laceration of cervix	13	8.9
Circumvallate placenta	9	6.1
Undetermined	6	4.1
Ruptured umbilical vein	2	1.4
Hemangioma of placenta	1	.7
Ruptured varix of vulva	1	.7

Vaginal Examination.—Proof that bleeding is due to placenta previa rests on palpation of the placenta directly over or within the finger's reach of the internal os. Though a closed cervix may not permit direct palpation of the placenta, strongly suggestive evidence may be obtained by palpation of the lower segment in the region immediately surrounding the cervix. If the presenting part is in the lower segment, an impression of very little tissue interposed between the finger and the fetal part practically rules out all types of placenta previa except the low-lying type, but a sense of bogginess and intervening tissue strongly suggests placenta previa.

Unfortunately, direct palpation of the placenta, which requires some degree of effacement and dilatation of the cervix, does not become available until near term, and further, it is well recognized that it is likely to provoke severe hemorrhage and force immediate definitive treatment. It seems more desirable, therefore, to postpone vaginal examination and to employ expectant treatment, if possible, to facilitate a later accurate diagnosis and ultimately to allow more intelligent definitive treatment.

Our increased use of expectancy in antepartum hemorrhage accounts for performance of only 17 vaginal examinations in 51 cases of placenta previa, revealing 2 complete, 3 partial, 4 marginal, and 8 low-lying placenta previas. In the remaining 34 cases, the diagnosis was based on (a) vaginal bleeding clinically consistent with placenta previa, (b) marginal rupture of the membranes, (c) definite placental evidence of previous marginal placental bleeding, and, frequently, (d) evidence of compression of the rim of the placenta by the presenting part.

Reconstruction of uteroplacental relations based on the site of the membrane rupture is of questionable accuracy.[10] However, the concept of a normally implanted placenta with a membrane defect extending to the placental margin is more readily acceptable than placenta previa with a centrally located defect. With this in mind, and in view of the somewhat high incidence of placenta previa in our series, we are impressed with the possibility that more accurate means of detecting placental site would reveal an even higher incidence of ruptured sinus in normal implantation and a lower incidence of previa. The use of membrane rupture site in this series has been chiefly to exclude low implantation in cases of rupture of the marginal sinus, though we feel it will be found that hemorrhage from this source is present likewise in placenta previa.

The use of x-ray must be considered an adjunct of increasing value in diagnosis of placenta previa.

Vaginal examination in cases of abruptio and painless hemorrhage in normal implantation is of value only in respect to noting the absence of placenta previa.

Examination of the Placenta.—In cases of antenatal rupture of the marginal sinus, study of the placenta shows old or recent clot adherent to a portion of the placental margin, overlying a tear in the marginal sinus, and spreading out over the adjacent membrane, and occasionally covering a narrow portion of the

maternal surface of the marginal cotyledons. Indentification of a rent or slit in the sinus wall is not pathognomonic of hemorrhage from it unless a thrombus is present in the sinus at the point of rupture in continuity with the adjacent old clot. It is conceivable that if the sinus rupture is recent, as during the late first or second stage of labor, the thrombus might not be seen or its continuity with the clot not convincing. A central rupture of the membranes presumably rules out placenta previa. When the rupture site is lateral or marginal, approaching the site of sinus rupture, the detection of low implantation depends more on vaginal examination or other findings previously mentioned.

Fig. 2.—View of placental margin, cotyledons above, membranes below, showing thin wall of marginal sinus at site of rupture, sinus thrombus, and, to right, portion of large adherent clot.
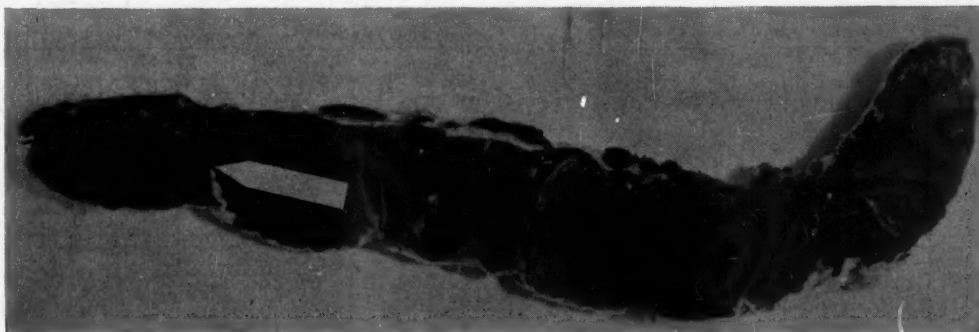
Fig. 3.—Formalin-fixed placental strip showing acute marginal infarct with central hemorrhage, confirming abruptio. Hemorrhage was entirely marginal and fresh specimen appeared similar to that in Fig. 2.

Abruptio, involving only a localized area on the margin of the placenta, may produce bleeding which simulates that due to rupture of the marginal sinus or vice versa. In addition to showing some manifestations of true toxemia, it is easily identified by the finding of an acute or subacute infarct within the placenta adjoining the site of hemorrhage. The mechanism by which poisonous

split-protein products, developing in infarcted placental tissue, might give rise to hemorrhage from the adjacent maternal sinuses and vessels has been discussed in a previous article.[11]

Considering other clinical comparisons, as to the stage of pregnancy at which bleeding occurs, it is true of placenta previa, abruptio, and rupture of the marginal sinus that the frequency increases in the third trimester and as term approaches. Fifty-eight per cent of sinus ruptures occurred in labor. In twelve per cent the hemorrhage remained concealed (Table II).

TABLE II. STAGE OF GESTATION OF UTEROPLACENTAL HEMORRHAGE

		PLACENTA PREVIA	ABRUPTIO PLACENTAE	RUPTURED MARGINAL SINUS
Month of gestation	6	2 (4%)	—	1 (2%)
	7	2 (4%)	—	3 (6%)
	8	9 (17.6%)	1 (7.1%)	3 (6%)
	9	12 (23.5%)	2 (14.2%)	8 (16%)
Intra partum		18 (35.2%)	5 (35.7%)	29 (58%)
Post partum		4 (7.8%)	—	—
No external bleeding		4 (7.8%)	6 (43%)	6 (12%)

There obviously exists no tendency to recurrence of bleeding in abruptio, since this condition either terminates or demands termination of pregnancy. As for placenta previa, it is nearly axiomatic that recurrent hemorrhage is inevitable. In 25 cases of previa manifesting the initial hemorrhage before labor, there were 14 recurrences, or 56 per cent, two of these following vaginal examination. Three out of 15 cases, or 20 per cent of cases of marginal sinus rupture, showed spontaneous recurrence of hemorrhage (Table III).

TABLE III. RECURRENT HEMORRHAGE INCIDENCE

	PLACENTA PREVIA		RUPTURED MARGINAL SINUS	
Bled before labor	25 cases		15 cases	
Bleeding recurred	14 (56%)		6 (40%)	
After vaginal exam.		2 (8%)		2 (13.3%)
In labor		1 (4%)		1 (6.7%)
Spontaneously		11 (44%)		3 (20%)

The character of bleeding observed in this series is tabulated in Table IV.

TABLE IV. CHARACTER OF BLEEDING

	PLACENTA PREVIA		ABRUPTIO PLACENTAE		RUPTURED MARGINAL SINUS	
Bled before labor	25		3		15	
Gross hemorrhage, bright blood		14 (56%)		2 (66.7%)		11 (73.3%)
Small bright hemorrhages		10 (40%)		—		3 (2.0%)
Dark blood with or without clots		1 (4%)		1 (33.3%)		1 (6.7%)
Bled during labor	18		5		29	
Bright, free flowing		8 (44.4%)		1 (20%)		8 (27.6%)
Bright, moderate excess ''show''		6 (33.3%)		—		10 (34.5%)
Dark blood with or without clots		4 (22.3%)		4 (80%)		11 (37.9%)
Concealed hemorrhage	4		6		6	

The bleeding of placenta previa is almost invariably bright, due to the immediate, unhindered escape of blood from a source near the cervix, which likewise lessens the tendency to formation of clots. That of abruptio, by contrast, is usually dark, more intermittent, and accompanied by firm dark clots

due to retention of the blood by placenta and membranes, and having its source in the upper part of the uterus.

In our experience, bleeding before labor from rupture of the marginal sinus most often simulates the hemorrhage of placenta previa in being sudden, profuse, usually of bright red color, without large clots, and subsiding in a few minutes. Occasionally, in normally situated placentas, bleeding from the marginal sinus may be retained for some hours by the membranes, with the ultimate escape of dark blood and clots and may thus simulate abruptio. This appears to pertain especially in labor, when previously concealed bleeding only then becomes manifest. It is in these cases that examination of the formalin-fixed placenta for acute infarction aids greatly in placing the case in the proper category.

Pain and shock are more characteristic of abruptio, due to the uterine rigidity, retained clots, and the toxemic nature of the condition. Pain is rarely present in ruptured marginal sinus and practically never present in placenta previa. Shock is present in ruptured marginal sinus and placenta previa only in proportion to excessive loss of blood.

Of 15 patients bleeding from ruptured sinus prior to labor in this study, one had mild continuous pain associated with minimal tenseness of the uterus for twelve hours before labor. There were no instances of shock.

Rigidity of the uterus is notably absent in placenta previa, seldom if ever present in ruptured marginal sinus, but frequently present in abruptio. While it is probably true that the presence of clots or fluid beneath the placenta or membranes may excite a mild degree of uterine tonicity, the marked degree of tonicity which characterizes so many cases of abruptio is more likely related to the presence of histamine, which is one of the probable breakdown products of placental necrosis. We have observed only two cases of ruptured marginal sinus which showed definite increase in uterine tone.

TABLE V. INTERVAL BETWEEN INITIAL HEMORRHAGE AND DELIVERY

	PLACENTA PREVIA	RUPTURED MARGINAL SINUS
Less than 24 hours		
At term	6 (24%)	4 (26.6%)
Before 38 weeks	3 (12%)	3 (20%)
Up to 3 weeks	6 (24%)	6 (40%)
3 to 6 weeks	6 (24%)	1 (6.7%)
6 to 12 weeks	4 (16%)	1 (6.7%)

TABLE VI. STAGE OF GESTATION AT DELIVERY

	PLACENTA PREVIA	ABRUPTIO PLACENTAE	RUPTURED MARGINAL SINUS
Term	40 (78.4%)	10 (71.4%)	35 (70%)
33-37 weeks	10 (19.6%)	3 (21.4%)	12 (24%)
Less than 33 weeks	1 (2%)	1 (7.2%)	3 (6%)

The nature of the pathology of abruptio placentae almost invariably causes or demands interruption of pregnancy. Painless, "causeless" hemorrhage has been considered pathognomonic of placenta previa, and until recent years pregnancies have been interrupted by operative or other means without delay. Experience with the expectant management of placenta previa, introduced independently by Johnson and Macafee, has shown that many patients can be carried to or near term without increase in maternal mortality and with greater salvage of fetal life.

Tables V and VI indicate a somewhat greater incidence of premature labor in the presence of rupture of the marginal sinus than in placenta previa, and also suggest a somewhat greater possibility of carrying previa expectantly for periods in excess of three weeks. Only two patients, of 15 who bled before labor from rupture of the sinus, continued their pregnancies for longer than three weeks. Twenty per cent of those who bled before term either terminated spontaneously or required termination of their pregnancies within twenty-four hours.

In respect to the effect of placenta previa, abruptio, and ruptured marginal sinus on the third and fourth stages of labor, it may be stated that postpartum hemorrhage is to be feared most in placenta previa, due to inadequate muscular control of bleeding from lower segment sinuses at the placental site. Postpartum hemorrhage in excess of 300 c.c. occurred four times in this series, each time associated with placenta previa. This represents 8 per cent of the previas.

In abruptio, the duration of the third stage is often decreased due to previous placental separation. The abruptio uterus is hypertonic and commonly contracts well, and postpartum hemorrhage beyond control of oxytocics is probably due to altered coagulability of the blood. Our experience with abruptio has not justified a fear of atony of the infiltrated, or Couvelaire, uterus.

There is apparently no predisposition to hemorrhage or alteration in the mechanism or duration of the third stage in cases of ruptured marginal sinus of the normally implanted placenta, and no instance of postpartum hemorrhage was encountered in the present series.

TABLE VII. TOXEMIA AND HEMORRHAGE, COEXISTENCE

	TOTAL CASES	CASES WITH TOXEMIA
Abruptio placentae	14	9 (64.3%)
Placenta previa	51	1 (1.9%)
Ruptured marginal sinus	50	4 (8%)

Evidences of toxemia are not present in instances of placenta previa or ruptured marginal sinus in any more than the expected frequency (Table VII). In abruptio placentae they are usually present, occasionally days or even weeks preceding the hemorrhage. They may, however, be entirely absent in fulminating cases until, or even after, the onset of the hemorrhage. These are the cases in which a probable histamine effect, arising from extensive acute infarction, damages the maternal vessels adjacent to the infarct, causing hemorrhage, separation of the placenta, and termination of the pregnancy before the usual manifestations of toxemia can develop. Close observation of the urine and blood pressure in the first few days of recovery may demonstrate a lagging development of some of the findings of toxemia.

TABLE VIII. MORTALITY

	FETAL			MATERNAL
	STILLBORN	NEONATAL	TOTAL	
Placenta previa	3	2	9.8%	None
Abruptio placentae	3	1	28.6%	None
Ruptured marginal sinus	–	2	4.0%	None

We have encountered no maternal deaths in this series of hemorrhages. Fetal mortality from placenta previa in this series is low. We are confident that considerable reduction in mortality has resulted from expectant management. The rate for ruptured marginal sinus, managed similarly, is less than half that for previa (Table VIII). This is in part due to less risk of placental

compression and consequent fetal embarrassment when the placenta is implanted normally. Both fetal deaths in rupture of the sinus were neonatal, and occurred in infants weighing less than 1,500 grams.

Management

Since abruptio placentae is of such a nature that it either brings about or requires termination of pregnancy, there can be no expectant manner of treating this condition. We have long been convinced that conservative treatment and vaginal delivery are preferable to cesarean section or accouchement forcé, not only from the standpoint of immediate risk but also of future risks in childbearing.

The abruptio patient is usually toxic, susceptible to and continually on the verge of shock, and is a poor surgical risk. Measures should be taken in advance to prevent shock and to combat it promptly by sedation and blood transfusion and by treatment of the toxemia. Labor may then be induced or stimulated by artificial rupture of the membranes and, if necessary, small doses (½ to 1 minim) of Pitocin.

An unprepared cervix, still having some length and little or no dilatation, is no contraindication to conservative treatment and does not constitute indication for cesarean section. As we have shown in a recent study,[11] such unfavorable cervices permit artificial rupture of the membranes and become effaced and dilated with surprising facility under the effect of natural or induced labor. It does not seem logical that a patient who happens to be seen first after the cervix is effaced and partly dilated, and therefore is considered favorable for conservative treatment, should be treated by cesarean section if she happens to have been seen first a few hours earlier, before the cervix has undergone these changes.

After the initial loss of blood has occurred with abruptio placentae, further loss tends to be limited by thrombosis of the sinuses, hypotension, and increased uterine tone. Close observation and supportive treatment are very important for some hours after delivery.

The prognosis for the baby is poor at best and the choice of treatment should not be unduly influenced by consideration for his safety. If the placental abnormality involves a considerable area, especially the central portion, of the placenta, the separation is likely to be complete and cause immediate death of the baby. If the infarction is on the margin of the placenta and of lesser extent, the extravasation of blood produces less separation and the baby may not be imperiled.

In the management of cases in which the hemorrhage is painless and the tentative diagnosis is either rupture of the marginal sinus or placenta previa, the arguments for conservatism and expectant treatment seem far to outweigh those for immediate interference, operative or otherwise, provided proper facilities are available.

If the hemorrhage occurs too early in the last trimester to permit a positive diagnosis of placenta previa on account of a closed cervix, the question arises as to whether one is justified in doing cesarean section at once, solely on the basis of a painless, "causeless" hemorrhage. It would not seem so, considering the fact that so many of these hemorrhages are, later on, found to be due to ruptured marginal sinus. A policy of expectant treatment for placenta previa has been in vogue over a sufficient period of time to demonstrate that the maternal mortality is not increased thereby and that more babies are salvaged, provided the mother is under close observation and facilities for blood replacement and intelligent obstetric management are available.

If this applies to placenta previa, it is even more applicable to ruptured marginal sinus for the following reasons: the placenta may be normally located, hence both placenta and cord are less liable to compression by the presenting part in normal labor, thus reducing the fetal risk in vaginal delivery; the hemorrhage is less likely to be recurrent; the nearer a patient can be carried to term, the more frequently may the cervix be found sufficiently patent to confirm or rule out placenta previa and thus permit a more intelligent decision as to the proper method of delivery.

Specifically, the management of painless hemorrhage of uncertain origin may be outlined as follows:

On admission to the hospital following the occurrence of a sudden, painless, "causeless" hemorrhage of considerable amount, the gravity of the patient's condition is quickly judged in terms of pallor, dyspnea, pulse, blood pressure, blood examination, and visible evidences of the severity of the hemorrhage from soiled clothes, towels, and pads. The active bleeding has usually ceased. The laboratory proceeds immediately with blood matching to bank or donor's blood.

Facts are quickly obtained in the history as to preceding evidence of toxemia, the presence of pain preceding or accompanying the bleeding, and the character of the blood or clots. Examination centers on the presence or absence of edema, rigidity and tenderness of the uterus, fetal position and engagement, and the presence or absence of fetal heart sounds and uterine contractions.

Preparation of the patient is limited to shaving and spraying locally with antiseptic. A catheterized specimen of urine is obtained for examination, but no enema is given.

Presuming the pregnancy to be at or near term, so that there is no element of fetal risk to be considered from the point of view of prematurity, two courses are open. The first is to proceed with evaluation of placental implantation site and possible delivery methods by making a vaginal examination.

If vaginal examination is decided upon, the patient is prepared as for delivery, ample blood (1,000 to 1,500 c.c.) is made ready, and intravenous fluids started slowly through a large needle. Sufficient facilities and assistance should be at hand to proceed immediately with whatever treatment the vaginal findings and other circumstances may indicate.

Light anesthesia for examination may be a time-saving and blood-saving measure should it facilitate quick resort to cesarean section, if indicated, or should it avoid interference on the part of the patient if painful manipulations are necessary in carrying out treatment preparatory to delivery by the vaginal route. The need of pre-anesthetic sedation should be anticipated.

It is obvious that if, on vaginal examination, the placenta cannot be found within reach of the examining finger within the internal os, delivery by the vaginal route may be planned. In general, the greater the proximity of the placenta to the cervical os, the stronger the indication for cesarean section in preference to the induction of labor and the control of hemorrhage by placental pressure methods.

Still presuming the hemorrhage to have occurred at or near term, the second alternative is to pursue an expectant course until or unless some definite contraindication thereto should arise, even though nothing is to be gained at this stage as to the baby's maturity. The onset of labor following the hemorrhage would constitute an obvious contraindication to expectancy.

There appear to be valid reasons for employing expectant management even at or near term. These are: (a) many gravidas approach term without good cervical effacement, and vaginal examination would lose value in the obscurity of a thick, closed cervix; (b) the possibility of intrapartum infection originating

in the medium of blood lying in the lower segment is greater if delivery, either abdominal or vaginal, is delayed for several days following examination than if delivery follows immediately; (c) vaginal examination increases the risk of subsequent hemorrhage and therefore would increase the risk of watchful waiting subsequent to such manipulation; (d) accepting, then, that for these reasons vaginal examination should be followed by some active steps toward termination of pregnancy, it becomes necessary to assume both the maternal and fetal risks associated with induction of labor should findings favor vaginal delivery; (e) finally, the high incidence of marginal sinus bleeding revealed in this study would appear to increase the safety of expectant management of hemorrhage no matter whether it occurs at seven months or at term.

Presuming the pregnancy to be in the seventh or eighth month, when prematurity greatly lessens the baby's chance of survival, what then is the preferable management?

It would seem desirable, under these circumstances, to employ expectant treatment if possible. The patient is hospitalized and prepared, but examined neither vaginally nor rectally. Blood replacement is carried out to whatever extent is required to re-establish a margin of safety in case of recurrent hemorrhage. The patient is kept under observation in the hospital two or three days on account of the possibility of the persistence or immediate recurrence of bleeding. Arrangements are made for donors for future use if there is no blood bank. The patient may then be discharged from the hospital with instructions to continue iron therapy, never remain alone, strictly avoid contamination of the vaginal tract, and arrange for prompt notification of the physician, hospital, and means of transportation in the event of another hemorrhage.

The question arises as to whether the patient's safety dictates continued hospitalization during expectant treatment. Considering the fact that the hospital offers no means of prevention or immediate control of the hemorrhage; that the hemorrhage quickly subsides and is rarely fatal provided a satisfactory blood picture is maintained, and provided there is not ill-advised tampering or examination; and that necessary preparations can be started while the patient is being transferred to the hospital, it would seem medically within the bounds of safety as well as economically desirable for the patient to be returned to her home.

Further hemorrhage may not occur, or after a variable interval, perhaps days or weeks, there may be a second episode. The patient is rehospitalized at once and the procedures previously mentioned are again carried out. If the baby's development is still not sufficient to be compatible with safe extrauterine life, another period of expectant treatment may be tried in an attempt to attain a stage of maturity more favorable to the baby and a stage of cervical preparation more favorable to accurate diagnosis and to vaginal delivery.

Expectant treatment is contraindicated (1) if persistent bleeding, even small in amount, continues day after day, rendering the patient anemic and predisposing to infection and poor resistance to further gross hemorrhage, or (2) if recurring hemorrhages are frequent, or of large amount, or (3) if the patient's blood is of a rare type, difficult to obtain in the blood bank or from anticipated donors, or (4) if the patient, living in poor surroundings with inadequate hospital facilities and professional aid, is unable to take up her residence elsewhere, in close proximity to competent attendants and good hospital facilities.

As has been stated before, vaginal and rectal examinations are deferred until expectant treatment, for any of the before-mentioned reasons, can no longer be carried on, or until natural labor occurs at term. The nearer to

term the pregnancy can be carried, the more likely it is that the condition of the cervix will allow satisfactory examination and thereby permit treatment to be based on accurate findings.

If labor starts and proceeds in its early stages without hemorrhage, there would appear to be no real indication for vaginal examination at any time. In such cases in this series, we have followed progress in labor with rectal examination without having encountered recurrent bleeding of any consequence.

At delivery, whether by section or by the vaginal route, the placenta should be delivered with as little trauma as possible, in the endeavor to preserve the natural relations of the membranes and their site of rupture to the placenta, and to avoid disturbance of adherent clots, thrombi, and other evidences of uteroplacental bleeding. This will aid greatly in confirming or establishing the diagnosis.

Conclusions

1. Rupture of the marginal sinus of the normally implanted placenta was found to be responsible for one-third of all cases of antenatal hemorrhage occurring in the last trimester or in labor.

2. Rupture of the marginal sinus, accounting for many of the antenatal hemorrhages heretofore classified as of unknown origin, closely simulated placenta previa.

3. The fragile membranous structure of the marginal sinus renders it susceptible to rupture under conditions of stress which would not, ordinarily, result in placental separation.

4. It is probable that rupture of the sinus, rather than placental separation, is the actual cause of bleeding in many cases of placenta previa, and can be demonstrated to be the usual cause in cases in which the placenta is normally implanted.

5. The frequency of antenatal hemorrhage due to ruptured sinus progressively increased in each successive month of the third trimester, but was highest during labor.

6. Placenta previa showed a higher incidence of bleeding before labor; ruptured marginal sinus a higher incidence of bleeding during labor.

7. Rupture of the marginal sinus showed a greater tendency to bring on labor than placenta previa, both at and before term.

8. Hemorrhage due to ruptured sinus showed less tendency to recurrence than placenta previa, but simulated placenta previa in respect to absence of pain and the bright and profuse character of the bleeding. Gross hemorrhage was more frequent in ruptured sinus than in placenta previa.

9. Evidence of associated toxemia was present in 64.3 per cent of abruptio cases, but was of no more than average incidence in placenta previa and rupture of the marginal sinus.

10. Of the three most important causes of antenatal hemorrhage of late pregnancy—rupture of the marginal sinus, placenta previa, and abruptio placentae—rupture of the marginal sinus was attended by the lowest fetal mortality (4 per cent). There was no maternal mortality.

11. Expectant management, of proved value to mother and fetus in placenta previa, is even more applicable to the hemorrhage of ruptured marginal sinus, in which the risk to mother and baby is much less, provided blood losses are replaced. It is not applicable to the hemorrhage of abruptio placentae since this condition is of a toxic nature, usually terminating or requiring termination of pregnancy at once.

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THE MANAGEMENT OF FIBROMYOMATA UTERI*

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FIBROMYOMATA uteri, or uterine fibroids, are the most common tumors to be found in the female. Novak[1] states that 20 per cent of women over 35 years of age have such tumors. The location of these tumors is extremely variable, and a number of symptoms may be caused by them. Likewise it is true that many fibroids are asymptomatic and the host does not recognize their existence. Frequently symptoms are attributed to fibroids when they are in no way related. The symptoms of fibroids per se are abnormal bleeding, pain, or pressure. The abnormal bleeding may be either menorrhagia, metrorrhagia, or polymenorrhea. Pressure results from the actual size and weight of the tumor and its effect on the contiguous pelvic structures. Pain represents circulatory disturbances of benign or malignant changes in the tumor. There has been a wide variety of opinion in regard to the management of fibroids. The present trend among gynecologists has been to manage these tumors in a conservative fashion in an effort to preserve the uterus and childbearing function. We have reviewed our cases of fibromyomata uteri in an effort to evaluate our own treatment. Have we been radical or conservative, and if so why?

Material

The cases reviewed in Table I are a consecutive group of white private gynecologic patients, with the exception of twelve obstetric cases which will be discussed separately. It should be pointed out that our practice consists mainly of consultative and referred work. Our patients are derived from two sources: physicians not connected with the Private Diagnostic Clinic, and specialists within the Clinic.

TABLE I. INCIDENCE

Total cases reviewed	4,077
Diagnosed fibroids	253
Incidence of fibroids	6.0%

We use the term "radical" as applying only to major surgery in which the uterus has been sacrificed. Observation or expectant treatment, myomectomy, and irradiation are considered conservative measures. We have divided our cases into six clinical groups and will consider the management of each.

Management

One hundred fifty-three patients with fibroids have been examined and advised that hysterectomy was not necessary but that they should be examined at regular intervals.

TABLE II. OBSERVATION, 153 CASES, INCLUDING 28 CURETTAGES

CHIEF COMPLAINT	UNDER 40 YEARS		40-44 YEARS		45-49 YEARS		50 YEARS AND OVER		TOTAL
	SMALL*	LARGE*	SMALL	LARGE	SMALL	LARGE	SMALL	LARGE	
Surgery advised	9	2	5	6	3	0	0	2	27
Cancerphobia	0	0	0	0	1	1	0	2	4
Bleeding	12	5	11	1	5	2	4	3	43
Pelvic check	24	9	9	6	5	5	3	1	62
Pain	5	4	1	3	4	0	0	0	17
Total	50	20	26	16	18	8	7	8	153

*"Small" designates tumors under 5 cm. and "large" over 5 cm. in diameter.

Table II is a breakdown into age groups, chief complaint, and the size of the tumor. It does not mean that only one tumor was present, as there were general ly multiple tumors, subserous, submucous, and intramural in position.

"Surgery advised" refers to those patients who had been advised elsewhere that a hysterectomy was necessary.

CASE 1.—An example of conservative management is the case of this 42-year-old patient who had a myomectomy in 1938 and a dilatation and curettage in 1940. She came to us because a hysterectomy had been recommended by her local physician. She was asymptomatic but appeared thin, worried, and depressed. One intramural fibroid, measuring 4 cm. in diameter, was noted on pelvic examination. She was advised that a hysterectomy was un-necessary. Three months later she returned in excellent spirits and with an increase in weight. She explained her improvement by saying, "I took the money I was saving for an operation and went to Florida for the first vacation in many years."

Cancerphobia was the chief complaint in only four cases. However, many other patients admitted their fear of cancer on further questioning. This fear was caused by the patient's knowing that a tumor was present or due to a previ-ous examiner's insisting upon an operation in order to prevent cancer.

Forty-three patients complained of abnormal bleeding. Twenty-eight of these patients were subjected to a diagnostic dilatation and curettage and were completely free of symptoms following this procedure. All of the postmeno-pausal patients fall into this group. Fifteen patients did not have sufficient evidence that they had been bleeding as much as the complaint indicated and, therefore, were not subjected to the curettage.

The largest number of patients fall into the group labeled "pelvic check." This includes patients whose chief complaints consisted of such symptoms as leucorrhea, pruritus, pelvic relaxation, etc. The majority of these patients were referred, some with the realization that they had a tumor, and some unaware.

Pain was an uncommon complaint. In nearly all of the cases pain could be ascribed to lesions of adjacent organs or other pathologic conditions of the geuital tract. Many of the patients were cured with the proper treatment.

CASE 2.—Mrs. D. S. (NCBH No. 29685) was 42 years old and was first seen June 21, 1944. She had a fibroid uterus which filled the pelvis and extended above the umbilicus. Multiple nodules, average 7 cm. in diameter, were present in all positions. Her chief complaints were hot flashes and abnormal vaginal bleeding. She was observed at intervals for four and one-half years, her last examination being in January, 1950. At that time she was two years postmenopausal and examination revealed one tumor measuring 4 cm. in diameter.

Table III illustrates the results of follow-up examinations. The term "im-proved" means that the tumor was stationary or decreasing in size and symptoms were no longer present. The patients listed under "unimproved" continue to have symptoms and/or exhibit an increase in the size of the tumors. Sixty-five

patients have not been followed by us but were advised to see their own physicians at regular intervals. Another example of conservative management is illustrated by the following case history.

TABLE III. FOLLOW-UP ON OBSERVATIVE CASES

DURATION OF FOLLOW-UP	SIZE	AGE IN YEARS								TOTAL
		0-40		40-44		45-49		50		
		IMPROVED		IMPROVED		IMPROVED		IMPROVED		
		YES	NO	YES	NO	YES	NO	YES	NO	
Under 1 year	Small	8	0	7	2	3	0	2	0	22
	Large	8	2	4	0	4	0	5	0	23
1 year	Small	9	0	5	0	1	0	0	0	15
	Large	2	1	4	0	2	0	2	0	11
3 years or over	Small	6	0	2	0	2	0	0	0	10
	Large	3	0	1	1	2	0	0	0	7
Total		36	3	23	3	14	0	9	0	88

Total cases	153
Total not followed	65
Total followed	88
Total improved	82
Total unimproved	6

Twelve myomectomies were done of which ten were abdominal procedures. This group includes four cases in which the tumors were removed incidentally to the primary operation. These tumors varied from 2 to 5 cm. in diameter. In the remaining six abdominal cases, a myomectomy was the primary operation and all of these tumors were over 5 cm. in diameter. These patients have been followed from five to fifty-two months and all are asymptomatic. Only one patient has had a recurrence.

Two prolapsing submucous fibroids, measuring 3 and 8 cm. in diameter, were removed per vaginam. The patient with the smaller fibroid also had an intramural fibroid 8 cm. in diameter. She has been followed for two years without any evidence of increase in the size of the tumor or any symptoms referable to it. The other patient has been followed for five years and the uterus is small and atrophic.

TABLE IV. MYOMECTOMY

Abdominal		10
Youngest	19 years	
Oldest	39 years	
Average	32.7 years	
Vaginal		2
Ages 45 and 48 years		
Mortality		0
Morbidity		8.3%
Complication		0

Three patients who had myomectomies are discussed in detail.

CASE 3.—Mrs. N. E. E. (NCBH No. 40149), a 33-year old white married mullipara, was first seen on May 30, 1945, complaining of pelvic tumors diagnosed by her family physician. Examination revealed an irregular, firm mass rising to the umbilicus, with numerous fibroids in all positions. A laparotomy was performed and twenty-five fibroids were removed. The largest measured 7 cm. in diameter and weighed 500 Gm. The endometrial cavity was entered and a submucous nodule was also removed. The pathologic report confirmed the diagnosis. The patient was observed over a two-year period during which time she had no symptoms and no

abnormalities were noted on examination. In December, 1947, she was found to be pregnant. Her prenatal course was uneventful and she was delivered in May, 1948, by abdominal cesarean section of an 8 pound, 6 ounce normal infant. The indication for the cesarean section was cephalopelvic disproportion. At operation the myomectomy scars were well healed, the uterine wall measured 3 to 4 cm. in thickness. Four small fibroids were felt in the anterior wall but were not removed. She was seen last one year later and the uterus was symmetrical without evidence of fibroids.

CASE 4.—Mrs. F. E. C. (NCBH No. 26052), a 31-year-old white married nullipara, was seen in March, 1944, with the chief complaint of infertility. She had been advised that she had a tumor of the uterus. On examination she was found to have a round, hard mass arising from the cervix and measuring approximately 10 cm. in diameter. The diagnosis of cervical fibroid was made and the patient advised that no surgery was indicated at that time. She was re-examined at three-month intervals and no change was noted until April, 1945, at which time the tumor was found to be enlarged with slight fixation and marked tenderness. In May, 1946, two years after the initial examination, a laparotomy was performed. The body and fundus of the uterus were identified anteriorly and to the left of a large fibroid arising from the cervix. During the attempt to shell out the fibroid, the lengthened cervical canal was completely transected at the level of the internal os. After the tumor had been removed and the bleeding controlled, a pack was inserted into the upper portion of the uterus and carried down through the transected canal into the vagina. The cervix was then sutured to the body of the uterus. Following the abdominal closure the patient was placed in the lithotomy position and the gauze packing was replaced by a plastic stem pessary which was anchored to the cervix. Two months later the patient reported that she had had two normal menstrual periods associated with only mild abdominal cramps. Examination revealed the uterus to be of normal size and a sound was passed to the depth of 2½ inches after the removal of the stem pessary. One year later a tubal insufflation was carried out successfully. She was asymptomatic three years after her operation and the uterus was found to be normal in size, symmetrical, and freely movable.

CASE 5.—Mrs. J. P. K. (NCBH No. 34283), a 19-year-old white unmarried nullipara, was admitted to the North Carolina Baptist Hospital in October, 1946, with the complaint of severe lower abdominal pain of seven days' duration. She had been hospitalized previously for abnormal vaginal bleeding in 1944 at which time examination was essentially negative, and a curettage revealed proliferative endometrial hyperplasia. On admission the abnormal findings consisted of a temperature of 101.4° F. and a mass in the lower midline extending 4 cm. above the symphysis. The mass was round, smooth, and measured approximately 5 cm. in diameter. Another mass measuring 10 by 5 by 4 cm., exquisitely tender, was felt in the cul-de-sac. The impression on admission was bilateral salpingo-oophoritis with possible pelvic or ovarian abscess.

Laboratory examinations, including cultures and a Friedman test, were all essentially negative except the white count which was 13,000. She was placed on penicillin therapy and her temperature subsided on the third day. Re-examination at this time revealed a definite fibroid mass and on the following day a laparotomy was done. The mass was located in the fundus of the uterus and dissection was carried down to the mass at which time a myoma measuring 12 by 10 by 10 cm. was located and removed. The center of the tumor showed an area of soft, dark red infarction. The uterine wall was closed in layers. She was last seen in July, 1949, three years after the operation. She had married and had one pregnancy which terminated in a spontaneous abortion at five months. Recent examination showed the uterus to be the size of a twelve-week pregnancy with some irregular nodules on the posterior surface. Further surgery was not advised.

Irradiation

Eight patients received irradiation therapy for treatment of their tumors. The predominating clinical features of the group were "flooding," small fibro-

myomatous uteri, and approaching menopause. Only one patient was younger than 45 and this patient was 38 years old. The largest uterus was the size of a three-month pregnancy. Three of the patients received x-ray irradiation in doses of 1,620; the remaining five received intrauterine radium varying from 1,500 to 2,400 mg. hr.

All but one of the patients were considered well on follow-up examination. She was unimproved and she was also the only patient who had any complications associated with irradiation.

Two of the cases deserve further mention. The younger patient ordinarily would have had a dilatation and curettage and no further therapy unless otherwise indicated. Her brother, a radiologist, insisted on the use of radium. The other patient's medical condition contraindicated laparotomy unless it was absolutely essential. She had a moderate menorrhagia and complained chiefly of severe lower abdominal pain. Following irradiation, she developed a pyometrium which has since cleared up. However, she still complains of her lower abdominal pain.

The relatively small number of patients treated by means of irradiation is due to several reasons. Irradiation does not always control the bleeding, as will be shown later. In addition, a very early carcinoma of the endometrium can be overlooked by the operator or the pathologist. Finally, since irradiation works by suppression of ovarian function, it is, in our opinion, to be avoided whenever possible.

Pregnancy

We have included twelve patients whose pregnancy was complicated by the presence of uterine fibroids. This small group does not represent all of the obstetric patients observed with tumors, but only those in whom the tumors were large enough to be referred for consultation in regard to management. Six of the patients had very large fibroids and were referred for interruption of pregnancy. All six were delivered vaginally, two by us. One case is reported in detail.

CASE 6.—Mrs. R. H. B. (NCBH No. 53924) was referred to the North Carolina Baptist Hospital for interruption of pregnancy and hysterectomy in the second month of her pregnancy. She was 34 years old, with a ten-year history of sterility. One year prior to her pregnancy she first noted a small lower abdominal mass. Five weeks after her last menstrual period the mass began to grow rapidly. On admission there was an abdominal mass arising to 16½ cm. above the symphysis. The mass was 19 cm. at its widest diameter. Her prenatal course was normal and uneventful until the fifth month at which time she developed abdominal pain in the left upper quadrant. A large tumor could be felt in the upper quadrant, impacted under the costal margin. The tumor gradually rotated from under the costal margin and the pain disappeared. She went into labor at term and after an eight-hour first stage and a thirty-one-minute second stage, she delivered a single footling weighing 8 pounds, 11 ounces. The third stage was five minutes in duration and associated with a blood loss of 600 c.c. The postpartum course was complicated by a very excessive lochial discharge which continued for eight weeks following delivery.

At the present time the patient has some lower abdominal pain and her menstrual periods are somewhat longer than usual. The tumor mass fills most of the lower abdomen and reaches to the umbilicus. She was last seen in January, 1950, and was advised to have a myomectomy if feasible.

Three patients each had a myomectomy in association with a cesarean section. Myomectomy was performed twice as an incidental procedure at the time a laparotomy was being performed for a ruptured ectopic pregnancy. One of these patients was first seen in the third month of a pregnancy with general-

ized peritonitis due to a necrobiosis of a uterine fibroid. She was treated conservatively without surgery and recovered. The pregnancy was terminated vaginally at term. One year later she had a ruptured ectopic pregnancy and a small fibroid was removed at that time. Two years later she aborted another pregnancy at two and one-half months. The final patient had a total hysterectomy and appendectomy for a fibroid measuring 10 cm. in diameter. An incidental finding was a 6 mm. embryo which was not suspected prior to surgery.

Malignancy and Fibroids

Five patients with malignancy are included in the series as they had associated fibroids. Two of these patients had multinodular fibroid uteri with carcinoma of the cervix. Both patients received x-ray and radium therapy for the carcinoma. One patient had adenocarcinoma of the fundus which was treated with intrauterine radium followed by a total hysterectomy and bilateral salpingo-oophorectomy. At operation a multinodular uterus with fibroids in all positions was removed.

The fourth patient had a total hysterectomy and a bilateral salpingo-oophorectomy for a multinodular fibroid reaching to the umbilicus and associated with excessive bleeding and persistent anemia. The pathology report showed no evidence of malignancy; however, one and one-half years later the patient had generalized ascites and a firm fixed mass in the pelvis. Laparotomy revealed a widespread carcinomatosis and a biopsy was diagnosed as papillary cystadenocarcinoma, probably of ovarian origin. The patient expired shortly thereafter.

The only instance of sarcoma in a fibroid in the group was in the fifth patient. It had been known for two years that she had a fibroid uterus. The mass increased rapidly in size and severe pain and tenderness developed. Under local anesthesia a subtotal hysterectomy was done. Two large tumors were found, one of which was diagnosed fibrosarcoma of the uterus. Postoperatively she did well for several months and then developed a pain in her chest and hemoptysis. A chest film revealed a tumor mass in the upper left lobe. A left lobectomy was done. The patient expired on the table. Pathologic examination revealed a metastatic fibrosarcoma. Autopsy was entirely negative for any other metastases and pelvic examination was entirely negative.

TABLE V. RADICAL TREATMENT

Total hysterectomy		43	
Subtotal hysterectomy		12	
Vaginal hysterectomy		4	
Total cases		59	
Mortality		0	
Morbidity	16.0%	**Complications**	10%
Urinary tract	6	Pelvic abscess	1
Pelvic peritonitis	1	Thrombophlebitis	2
Pelvic abscess	1	Bronchopneumonia	1
Thrombophlebitis	1	Atelectasis	1
Atelectasis	1	Peritoneal occlusion cyst	1

Table V is a composite table of all the radical surgery for fibroids including those patients with malignancy and pregnancy. The mortality is zero but the series is far too small to be significant. The morbidity was 16.9 per cent, mainly due to urinary tract infection. There were 10 per cent postoperative complications. The pelvic abscess occurred after a vaginal hysterectomy. The peritoneal occlusion cyst occurred one year postoperatively following a total hysterectomy. The patient was reoperated upon and is now well.

Mass.—In twenty-four cases, a hysterectomy was done for the presence of a mass which had been noted by a physician or the patient. In the majority,

the associated complaints were of a minor nature and probably unrelated to the tumor. Six patients in this group presented a differential diagnosis from ovarian tumor. Four of these had large pedunculated tumors, varying in size from 5 to 11 cm. in diameter. The other two cases were in the youngest, aged 27 years, and the oldest, aged 71 years, patients in the hysterectomy group. They had large intramural fibroids which measured 18 by 15 by 11 cm. One patient with papillary cystadenocarcinoma was mentioned in the malignancy group.

In the remaining 17 cases we question whether the operation was justified. Six patients had tumors averaging 10 cm. in diameter, but were not observed for a long enough period before the operation was performed.

On the insistence of an internist, two patients had hysterectomies performed in an effort to reduce their hypertension. There was a slight hydronephrosis in one case, the other being normal. The hypertension was not relieved in either patient. One patient was unable to wear a kidney ptosis belt because of the lower abdominal mass. Seven patients had cancerphobia as the main indication for the removal of their tumors. All of these patients had been advised against surgery. However, at the insistence of the patient, psychiatrist, or family doctor, surgery was finally done in all of them.

CASE 7.—Mrs. D. P. H. (NCBH No. 13572), a 41-year-old para i, was admitted to the psychiatric service with a diagnosis of hysteria. Her history revealed that ten years previously she had had appendectomy at which time some fibroids were removed. She was repeatedly advised that she should have a hysterectomy although her internist objected strenuously. A dilatation and curettage were done for abnormal bleeding and again the surgeon recommended a hysterectomy. She began to have fainting spells lasting from a few hours to a few days. She was sent to a sanatorium for treatment and remained in the institution for a period of three months. She was again seen by three physicians, one a gynecologist, who recommended immediate operation. She was also thoroughly investigated for the possibility of a brain tumor. For the next year she was treated off and on with various estrogenic hormones, but was unable to leave her home or even be out of bed for long intervals. At the insistence of a psychiatrist a total hysterectomy and perineorrhaphy were done. The uterus measured 11 by 7 by 4 cm. and contained several 2 cm. intramural fibroid nodules. The patient was then left in the hands of the operator, who spent numerous hours the next few years convincing her that all her troubles had been removed.

The hysterectomy in which a small embryo and placenta were found has been mentioned under pregnancy. It is debatable whether one would have operated if pregnancy had been suspected.

Bleeding.—Twenty-one patients were operated on because of abnormal bleeding. Twelve of these patients were 40 years old or over and had tumors larger than the size of a four-month pregnancy. One patient had a submucous fibroid and had failed to improve with a dilatation and curettage. Three patients had received castration doses of radium without cessation of the bleeding previously.

We do not believe that the operation was entirely justified in the remaining five cases. Two of the patients were found to have an endometrial polyp at the time of hysterectomy. It is probable that this was missed when the minor operation was done. Two patients had tumors 5 and 10 cm. in diameter, respectively. A dilatation and curettage were not carried out prior to the hysterectomy which might have saved both patients from major surgery.

Pain and Pressure.—Pain and/or pressure were the chief reasons for operation in ten patients. Six of them had marked bladder symptoms and associated pelvic relaxation. Four of these were managed by vaginal hysterectomy with plastic repair. In the remaining two cases the contour of the bladder, as determined by cystoscopic examination, was definitely distorted and both patients

were relieved of their symptoms following hysterectomy. The patient with sarcoma, who has been mentioned in the malignancy group, had as her chief complaint pain in the lower abdomen.

In three cases the operation does not seem justifiable on the basis of the tumors alone. In one case dysmenorrhea was the chief complaint and a 6 cm. intramural fibroid was found. In a second patient, the main indication for the operation appears to be primarily to remove a badly diseased cervix. The final patient had a fibroid 6½ cm. in diameter removed because of lower abdominal pain. The appendix was removed at the time of hysterectomy and revealed hydrops and a healing appendicitis which probably accounted for her symptoms.

Rapid Growth.—Rapid growth occurred in three patients who had been under observation for one, two and one-half, and four and one-half years, respectively. The tumors were estimated in all three to have doubled their size and severe bleeding was associated in each case. One of the tumors showed benign degeneration, the remainder were uncomplicated.

TABLE VI. AGE GROUP AND REASONS FOR OPERATION

REASON FOR OPERATION	AGE IN YEARS				TOTAL
	UNDER 40	40-44	45-49	50 AND OVER	
Mass	8	8	7	1	24
Bleeding	5	5	7	4	21
Pain	4	2	2	2	10
Rapid growth	0	2	1	0	3
Carcinoma of fundus	1	0	0	0	1
Total	18	17	17	7	59

Recommended Operation.—Eight patients were sent back to their referring physicians with the advice that hysterectomy should be done. In all cases the fibroids were large and there were associated symptoms which were felt sufficient to indicate the procedure.

TABLE VII. MANAGEMENT, 253 FIBROIDS

Conservative			186
Observation			
Tumors alone (includes 28 D & C)		153	
Tumors and pregnancy		6	
Myomectomy			
Tumors alone		12	
Abdominal	10		
Vaginal	2		
Tumors and pregnancy		5	
Abdominal	5		
Irradiation			
Tumors alone		8	
Tumors and malignancy		2	
		186	
Radical			67
Tumors alone		55	
Total hysterectomy	40		
Subtotal hysterectomy	11		
Vaginal hysterectomy	4		
Tumors and malignancy		3	
Total hysterectomy	2		
Subtotal hysterectomy	1		
Tumor and pregnancy		1	
Total hysterectomy	1		
Recommended removal		8	
		67	253

Comment

The most striking finding in this study has been in the group labeled "observation." Eighty-eight patients have been followed and have required no radical surgery. Eighty-two of these have not only avoided surgery, but have improved. This seems particularly fortunate in that twenty-seven of the patients in this group had previously been advised elsewhere that an operation was necessary. We believe that the majority of surgeons, some in our own specialty, are still unwilling to accept the fact that most uterine fibroids cause no symptoms and can be managed by observation alone.

Myomectomy must always be considered in a woman of childbearing age with fibroids requiring interference. Our series is small but seems to demonstrate that extensive surgery can be performed on a uterus without destroying its usefulness.

There has been only one case of sarcoma occurring in a fibroid in this series, a fact which coincides with the findings of others. The incidence of sarcoma is just as low as the operative mortality for hysterectomy. This fact cannot be emphasized too strongly since it should reduce the urgency for surgery.

We have performed or recommended hysterectomy in sixty-seven cases, or 26.4 per cent. This is approximately one in every four cases seen in a consultative practice of only white patients. A critical review of our findings in the operative group correlated with the symptomatology seems to indicate that in twenty-six cases the operation was not wholly justified. Exclusion of these cases would have reduced the incidence of surgery to 16 per cent. Neither the size of the tumor nor the age of the patient need be considered in the expectant treatment, as most tumors will regress in the postmenopausal period. Rapid growth, bleeding, pain, and marked pressure symptoms seem to be the most reliable signs indicating surgery.

Conclusion

At the beginning of the study we asked ourselves a question. "Is our management of fibroids radical or conservative?" In conclusion, we feel that in the past the management has been relatively conservative and as a consequence our patients have benefited. However, it is also apparent that the conservative approach could have been extended further with equally good results.

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ROUTINE ANTENATAL CHEST X-RAY FINDINGS IN PATIENTS DRAWN FROM A CURRENTLY SURVEYED POPULATION*

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X-RAY examination of the chest is recognized as an important adjunct to other steps in the appraisal of the pregnant woman's state of health.[1,2,8] Roentgenography is admittedly superior to other brief routine measures of examining the chests of apparently healthy individuals, particularly as regards the selection of patients, some of whom upon subsequent investigation may be found to have tuberculosis.[3,4,5] During the past decade photofluorography has afforded a method of diagnostic screening, applicable to large groups, that has minimized items of expense in materials, time, personnel, and space.

Bearing in mind the fallibilities inherent in technique, interpretation, recording, reporting, and follow-up, one may speculate as to how useful, how costworthy and how dependable may be this procedure in automatic mass use among antepartum patients. Has it a high yield of discovered lesions not otherwise detected or formerly known? Conversely, is a single routine examination adequately sensitive in terms of disease, manifest shortly afterwards, that may have been overlooked due to coarseness of the screening mechanism?

It is felt that the conditions under which the present study has operated afford a unique opportunity to assay the findings from a chest x-ray screening of nearly one-half of resident obstetrical cases, over a three-year period, in a community of about 100,000 population, wherein has been conducted concurrently a continuous study of tuberculosis among the entire population of the county.

The Columbus-Muscogee County Health Department, assisted by the Georgia Department of Public Health and the United States Public Health Service, initiated the county-wide tuberculosis study with a mass x-ray survey in May-June, 1946. In September of that year a house-to-house census was taken and all inhabitants were listed by sex, race, and age on household rosters.[6]

From July, 1946, forward, the continuous tuberculosis program has included intensive investigation of all contacts, suspects, and diagnosed cases, variously by means of microfilms, 14 by 17 x-rays, skin tests, bacteriological methods, medical consultation, home nursing visits, ambulatory outpatient clinics, and domiciliary care in the sanatorium or the central state hospital.[6]

The population of Muscogee County by the census of September, 1946, in round numbers was 96,500, of which 70 per cent was white and 30 per cent Negro. The number of enumerated women, aged 15 to 44 years was 28,088. On the initial survey 19,724 of them (70 per cent) were x-rayed.[7] This coverage has been increased in the three years following the survey, to an estimated 85 per cent of all women of childbearing ages.

The health department operates a prenatal center, as the outpatient branch of the Columbus City Hospital Obstetrical service. During this study period the number of antepartum admissions was equivalent to 31 per cent of the county's resident births. Nearly one-half of clinic registrants had hospital staff confinements; about one-fourth employed private physicians; and about one-third used midwives under clinic and nursing control, with hospitalization for abnormalities.

Since early 1944 the prenatal clinic has taken a microfilm chest x-ray of each patient, the day of admission. The service likewise has been rendered to all referred patients of private physicians. This study embraces the findings among 3,576 prenatal patients routinely screened during the three years, Aug. 1, 1946, through July 31, 1949.

The sources of x-ray referral of these patients were the clinic in two-thirds of cases, and private practitioners in one-third.

Patients Examined; Extent of Coverage

Table I shows the 3,576 patients x-rayed prenatally, compared with the total number of resident births, live and still, occurring in the country for the three-year period, classified by attendant at delivery. Repeat pregnancies are included in both compilations. The category "service" includes 1,027 hospital staff cases and 838 midwife cases.

The number of routine antepartum microfilm x-rays is equivalent to 46 per cent of the total resident births. Our study apparently reaches private patients to an extent equivalent to 29 per cent of the privately attended resident births in the county.

TABLE I. ANTEPARTUM PATIENTS X-RAYED AND TOTAL RESIDENT BIRTHS, SAME PERIOD, ACCORDING TO ATTENDANT AT DELIVERY

ATTENDANT	NO. BIRTHS L.B. & S. B.	NO. CASES X-RAYED	COVERAGE
Service	1865	1865	100%
Private	5932	1711	29%
Total	7797	3576	46%

Screened Cases Recalled and Findings on Further Study

Table II shows the numbers and per cent of screened cases recalled for investigation, according to the type of disease suggested by the microfilm. Four per cent of all patients gave evidence of chest lesions warranting diagnostic study. The pursuit and examination of patients recalled for possible tuberculosis was intensive and thorough. This was made possible by the concurrent tuberculosis study, well staffed, and with an efficiently indexed registry.

In the case of nontuberculous pathology, however, these advantages applied only as regards records and correspondence. Follow-up by mail and through private physicians could be supplemented by a search for recalcitrants only infrequently. Consequently the inadequately studied group consists almost exclusively of those having nontuberculous conditions.

In Table III are given the findings on restudy of 143 recalled patients. Possible tuberculosis was the reason for recall in 58 cases; all but one were adequately studied. Pulmonary tuberculosis was diagnosed 43 times or in 1.2

per cent of all cases of pregnancy screened. The 43 diagnoses were made in 37 individuals, four of whom had two pregnancies each, and one contributed three during the study period.

The prevalence of tuberculosis was slightly higher among white gravidas, the reverse of the findings among women in the general population on survey. This difference is explainable by a disparity in age distribution as between pregnant women of different races. The Negro gravidas are heavily weighted with younger women in whom the prevalence of the disease is lower.

Nontuberculous Pathologic Conditions

Mass photofluorography has assumed so much importance as a method of tuberculosis case finding, that the discovery of other diseases of the chest is viewed often as an incidental by-product. Of the 143 screen-selected cases shown in Tables II and III, 85 were recalled for investigation of possible intrathoracic lesions of a nontuberculous nature. Unfortunately, our limited facilities of pursuit have relegated their study to the by-product category, in that only 55 could be followed sufficiently well to arrive at a reasonably dependable clinical diagnosis.

TABLE II. X-RAY FINDINGS IN 3,576 PRENATAL CASES BY RACE AND TYPE OF LESION SUSPECTED. NUMBERS AND PER CENT RECALLED FOR INVESTIGATION

FINDINGS SCREENED CASES	NUMBERS			PER CENT RECALLED
	WHITE 1669	NEGRO 1907	TOTAL 3576	
Tuberculosis	27	31	58	1.6%
Cardiovascular	16	43	59	1.6%
Other lesions	15	11	26	0.8%
Total cases recalled	58	85	143	4.0%

TABLE III. DIAGNOSES IN 143 SCREENED PRENATAL CASES RECALLED FOR INVESTIGATION BY RACE AND BY TYPE OF DISEASE. PER CENT ABNORMAL OF TOTAL PRENATAL GROUP

DIAGNOSES	NO. WHITE	NO. NEGRO	TOTAL	% OF ALL PRENATAL CASES
Cases recalled	58	85	143	4.0%
Tuberculosis or suspect	22	21	43	1.2%
Cardiovascular	4	21	25	.7%
Other pathology (significant)	3	2	5	
Nonsignificant or normal	13	26	39	
Inadequately studied	16	15	31	

Twenty-five of these were designated as being normal, or having minor abnormalities of no clinical significance, or transient acute illnesses that resolved prior to the follow-up study. This leaves 25 with cardiovascular and 5 with other nontuberculous diseases of clinical importance as follows:

Congenital heart disease	6	
Rheumatic heart disease	10	
Hypertensive cardiovascular	8	
Unclassified cardiovascular	1	
Total cardiovascular		25
Sarcoidosis	3	
Nontuberculous infiltration (fungus?)	1	
Hilar tumor	1	
Total (other)		5

Combined, these conditions have a prevalence among the 3,576 prenatal cases of one in 119. We hope to study lesions of this type more appropriately in the future, particularly the hypertensive group. In more than an occasional case the x-ray clinician's report antedates any recorded clinical sign.

Antepartum Tuberculosis

It seems appropriate to test the effectiveness of the screening mechanism by comparing the positive tuberculosis findings of the study to the probable number of tuberculosis cases among all pregnant women resident in the community, to whom the facility is available (and actively promoted) regardless of whether or not they used it. We have taken, as an exposed-to-risk group, all mothers who gave birth to infants, liveborn and stillborn, in the county during the three years of the prenatal study.

The distribution of 7,797 resident births, by race and by age of the mothers, is shown in Table IV. Repeat pregnancies are included. The appropriate prevalence rates of tuberculosis, from the survey, are applied to these known gravidas, to obtain a theoretical expected number, amounting to 50 cases, probably present among the pregnant women of the community. This tuberculosis potential is exaggerated somewhat by the inclusion of repeat pregnancies. The opposite effect is contributed by the absence of pregnancies terminating prior to the fifth month, of which there are no reports for the community at large.

Cases of tuberculosis in this table are counted by individuals, omitting six repeat pregnancies among the "positive" cases. As compared to a probable number of 50 cases existing, 37 individuals were found with pulmonary tuberculosis, or strongly suspicious, during their antepartum periods. It would seem, then, that by the chest x-ray screening of 46 per cent of the pregnant women in the county, evidence of tuberculosis was found in a number equivalent to 74 per cent of the estimated probable total number of tuberculous gravidas in the area.

TABLE IV. TUBERCULOUS PREGNANT WOMEN. NUMBER DIAGNOSES, COMPARED TO NUMBER AMONG RESIDENT GRAVIDAS EXPECTED FROM AGE-RACE PREVALENCE (SURVEY AT START OF 3-YEAR STUDY)

MOTHER'S RACE AND AGE IN YEARS	NO. BIRTHS	SURVEY RATES	NO. EXPECTED	NO. DIAG.
White.—				
15-24	2598	.0017	4.4	5
25-34	2130	.0082	17.5	10
35-44*	468	.0151	7.1	5
Subtotal	5196		29.0	20
Negro.—				
15-24	1613	.0050	8.1	8
25-34	832	.0123	10.2	9
35-44*	156	.0173	2.7	0
Subtotal	2601		21.0	17
Total	7797		50.0	37

*Includes mothers over 44 years of age.

This high "yield" is magnified by two selection factors: (1) Most private physicians referred for x-ray study only those patients in whom history, symptoms, or findings suggested possible intrathoracic disease. (2) Even more potent is the effect of the community-wide tuberculosis search wherein a case, or suspected case, discovered variously, could hardly miss being verified by x-ray during a current or subsequent pregnancy. For example, 18 of the 37 individuals with diagnosed cases were known to the tuberculosis service prior to their prenatal admissions.

Table V shows the status of these patients regarding a knowledge of their disease prior to the antepartum x-ray. Nine cases were entirely newly discovered by the prenatal study. Among these, three were classed as suspicious, three as minimal inactive, two minimal active, and one advanced active disease. Of the five patients previously known elsewhere, but not to their attendants, three were found on antepartum x-ray to have re-activated cases, one advanced.

TABLE V. TUBERCULOSIS IN 37 PREGNANT WOMEN. STATUS OF KNOWLEDGE OF DISEASE PRIOR TO PRENATAL CHEST X-RAY

Known to Health Dept. or local doctor	23
Known elsewhere. Not under observation	5
Entirely unsuspected	9
Total	37

It is obvious that in these 12 patients the routine employment of an antepartum screen microfilm was of critical importance, and, adding the other two, the method is credited with the discovery of 14 cases. Thus, in the experience of our study, the routine has yielded significant evidence of pulmonary tuberculosis not otherwise suspected by the attendant, in one out of 255 cases. This is under conditions of unusual opportunity for tuberculosis to be discovered in other ways than through prenatal referral.

The 43 cases are given in Table VI according to the stage of disease and probable degree of activity (condensed categories). Over one-half as minimal and over one-third as moderately or far advanced, plus probable activity in two-fifths, is an indication of the significance of what was classified as tuberculosis.

TABLE VI. TUBERCULOSIS IN 43 PREGNANCIES BY STAGE AND PROBABLE ACTIVITY (CONDENSED)

STAGE	ACTIVE	INACTIVE	TOTAL	% DISTRIBUTION
Suspect	—	—	5	12%
Minimal	4	19	23	53%
Advanced (mod. and far)	10	5	15	35%
Total	14	24		
% Dist.	37%	63%		

Tuberculosis Diagnosed Following Childbirth

The elements of negative error and of nonapplication are qualities of any routine mass-applied technique that are difficult to assess, and often not reckoned. So far as concerns tuberculosis, it was possible in this study to secure information as to cases discovered by the community study, following a childbirth, that were either interpreted as negative on antepartum examination, or that received no x-ray referral during the pregnancy.

There were identified ten such patients, five in each category. None of the ten was suspected of the disease prior to delivery. These cases are listed in Table VII showing race, age, stage of disease, activity, and the number of months post partum when diagnosed.

At least five of these patients might well have had the disease during pregnancy. The remaining five cases were diagnosed more than four months after confinement; all of them were active cases, however, and in three the pulmonary lesions were far advanced. The case diagnosed as far advanced 20 months post partum, on retrospective review of the prenatal microfilm, was seen to show evidence of a small infiltration that was overoloked at the time. Therefore, it is quite possible that in all ten there was association between the pregnancy and the disease.

There were five cases with no visible lesion on antepartum x-ray, as compared to fourteen cases initially discovered by the procedure. This seems to indicate that for every three cases disclosed by routine screening during pregnancy, and otherwise undetected, there may be overlooked one in which serious illness becomes manifest disconcertingly soon following confinement. Or, put another way, of 42 pregnant women with tuberculosis, or soon to develop the disease, a single picture taken during pregnancy failed to warn of this danger in one out of eight.

Of the 43 pregnant patients in whom tuberculosis was diagnosed ante partum, 29 were x-rayed in the first trimester, 13 in the second, and 1 in the third. Among the 5 whose prenatal x-rays were interpreted as negative, these examinations were made during the first trimester in two and during the second trimester in three.

TABLE VII. TEN CASES OF TUBERCULOSIS DIAGNOSED AFTER DELIVERY

RACE	AGE (YEARS)	STAGE	ACTIVE	POST PARTUM
Negative Prenatal X-ray.—				
W	22	Far adv.	Yes	4 mo.
W	34	Far adv.	Yes	20 mo.
W	35	Min.	Yes	10 mo.
W	20	Min.	Yes	3 mo.
N	26	Far adv.	Yes	8 mo.
No Prenatal X-ray.—				
W	19	Far adv.	Yes	2 mo.
W	24	Min.	Yes	7 mo.
W	27	Min.	Yes	4 mo.
N	19	Suspect		1 mo.
N	28	Far adv.	Yes	12 mo.

Outcome of Pregnancies

Table VIII lists the 43 cases of antepartum tuberculosis and 10 cases discovered post partum, in accordance with the outcome of pregnancy and the early fate of the mothers and of those infants who survived the neonatal period. Despite the small numbers involved, the difference between the antepartum- and postpartum-diagnosis groups is striking. One mother in the former group died 6 months post partum, and five others were hospitalized beyond the puerperium; the remainder are under ambulatory observation. Among the 10 cases not diagnosed prenatally, eight required hospitalization when discovered. Three patients are dead, and four still in the hospital.

TABLE VIII. OUTCOME OF PREGNANCY. 43 CASES OF ANTEPARTUM TUBERCULOSIS AND 10 CASES DIAGNOSED POST PARTUM

OUTCOME	DIAG. ANTE PARTUM	DIAG. POST PARTUM
Moved, untraced	3	0
Not yet delivered	4	0
Therapeutic abortion	0	0
Spontaneous abortion	3	0
Stillbirth or neonatal death	3	0
Live birth	30	10
Total	43	10
Infants died of tuberculosis at 5 mo. and 6 mo.		2
Mothers died of tuberculosis at 6 mo., 7 mo., 13 mo., and 3 yr. P.P.	1	3

Among the 43 pregnant patients with known tuberculosis, seven were undelivered, or the outcome unknown at the time of compilation. There were

three spontaneous abortions, but no therapeutic interruptions. There were two premature stillbirths and one death at 9 hours of a term infant, the cause being certified as erythroblastosis. Of thirty liveborn infants, one died at 6 months of miliary tuberculosis; the remaining 29 were alive at the time of compilation. Among the 10 live infants born to the mothers whose tuberculosis was diagnosed post partum, two died within six months, of tuberculous pneumonia and tuberculous meningitis, respectively.

The foregoing findings indicate that certain patients with a single normal chest x-ray during early to mid-pregnancy, may develop, not too remotely post partum, pulmonary tuberculosis to a significant degree as to both frequency and severity. Further, the outlook for mothers and liveborn infants in such cases is fraught with disaster. The numbers here considered are small. It is felt, none the less, that they strongly suggest the advisability of securing a second microfilm in all cases, near term or during the lying-in period, or preferably on some practicable postpartum occasion such as the 6- to 8-week visit.

Summary

1. Analysis is made of the findings on routine chest photofluorography in 3,576 pregnancies. The cases examined were equivalent in number to nearly half of all resident gravidas in a county of 100,000 population, simultaneously undergoing survey and study of tuberculosis.

2. Four per cent of all patients showed sufficient signs of abnormality to warrant investigation.

3. Thirty cases of clinically important nontuberculous pathologic conditions were diagnosed, principally cardiovascular disease, a proportion of one in 119 of the total cases.

4. There were 37 women with 43 pregnancies in whom pulmonary tuberculosis was diagnosed ante partum; one for every 83 cases examined.

5. The single microfilm screening of all prenatal referrals resulted in the discovery of tuberculosis, not suspected by the obstetrician, in 14 women or one in 255. The remaining cases diagnosed were either known previously, or referred as suspicious.

6. There were found 10 cases of pulmonary tuberculosis, diagnosed from one to twenty months post partum, never previously suspected. Five of these patients had been reported as normal on the screening examination. Thus, among 42 individuals with tuberculosis in pregnancy, or shortly to develop the disease, our routine screening mechanism failed to yield a warning in one out of eight.

7. Comparison of the prenatally diagnosed group with those whose cases were discovered post partum shows a marked difference in fatality, with a more disastrous course of the disease in both mothers and infants among the latter group.

8. Our findings support the view that x-ray examination of the chest in all pregnancies is a highly useful procedure in terms of newly discovered tuberculous lesions otherwise unknown to the obstetrician.

9. Additional value of the method is attested by the frequency with which nontuberculous thoracic pathology of clinical importance is disclosed. Cases of this nature deserve more investigation than was possible in this study.

10. Despite the small numbers involved, our findings indicate that a single chest x-ray, in early to mid-pregnancy, is an insufficient sample upon which to assume that clinically important disease is unlikely to develop later in pregnancy or subsequent to delivery. The need for a supplementary examination of all patients, about the time of the initial postpartum visit, is suggested.

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Discussion

DR. ALBERT J. KELLEY, Savannah, Ga.—Dr. Bickerstaff has again brought to our attention a problem of interest to obstetricians, public health workers, and social workers. He has shown that in Columbus, Ga., routine chest surveys discovered 9 previously unsuspected cases of tuberculosis in 3,576 individuals screened.

In one of the first mass population surveys of the country, which was conducted in Savannah and Chatham County in 1945, a total of 38,201 women were screened. In this group there were found a total of 82 cases of tuberculosis, or approximately two per thousand. In 1948, the Chatham County Health Department began routine chest screening of all patients in prenatal clinics. In two years there were a total of 1,531 patients x-rayed. Of these, seven were found to have tuberculosis, but all seven cases had previously been diagnosed. No new cases were discovered.

Dr. Bickerstaff quotes a total tuberculosis rate or *suspect* tuberculosis of 1.2 per cent of all cases, some of which were previously diagnosed. His figures agree with those of Eisele and Mason, who found a tuberculosis rate of 1.06 per cent in six thousand odd patients at Chicago Lying-in Hospital. A later report by the group at Chicago Lying-in shows approximately the same incidence in ten thousand odd cases.

The National Tuberculosis Association has long urged routine screening of all patients admitted to hospitals. If this were followed through perhaps some previously unsuspected cases would be found at the time of delivery.

Tuberculosis certainly is a dread disease, and much to be feared in the pregnant woman. It is my belief, however, that the results heretofore shown hardly justify routine screening of all pregnant women, both clinic and private. It would seem to me that the effort should be more toward the screening of industrial groups and the diligent follow-up of all cases with very careful screening of all contacts of these patients.

DR. HAROLD G. NIX, Tampa, Fla.—The unique feature of this study is the fact that it was carried on currently as a prenatal survey in a county-wide study of tuberculosis in the entire population. As is shown in Table V, the vast majority of positive cases revealed by this study are either proved or suspected cases before the screening test.

One of the surprising features of this report is the much higher incidence of serious pulmonary disease shown by the postpartum examinations. If one should embark on a policy the routine studies reported from Hillsborough County had been carried out in a private partum than ante partum. We are all cognizant of the frequent exacerbation of an otherwise inactive or minimally-active tuberculosis in postpartum women.

The Hillsborough County Health Department has embarked on a similar routine of photomicrofilming of all patients registered in the prenatal charity clinic. In 1949 eight hundred thirty-two maternity patients had such a study. Of this number, sixteen revealed sufficient abnormal findings to warrant further study with the 14 inch by 17 inch chest x-rays, as well as clinical studies. Only one case of minimal inactive tuberculosis was found, but there were three cases of cardiovascular disease discovered.

My opinion is that there are grounds for questioning the practicality of routine radiographic studies of all antepartum and postpartum patients because of the small incidence of significant, unsuspected disease in comparison to the economic cost in private practice. If the routine studies reported from Hillsborough County had been carried out in a private radiologist's office, on private patients, the minimum cost would be $8,320.00 to uncover one case of minimal inactive tuberculosis. It is my opinion that in private practice the thorough history taking, combined with complete physical examination, will usually reveal those cases which warrant further radiographic study. It is true that clinic patients are handled in larger volume with less individual attention. It is also recognized that the incidence of tuberculosis is higher in those individuals of the lower economic scale.

DR. HOMER L. PEARSON, JR., Miami, Fla.—Similar surveys have been made elsewhere with about the same findings. Such surveys are of value if for no other reason than to enlighten us on the subject studied. The questions which, of course, arise are, "Are such studies feasible from an economic standpoint?" and, if so, "Should they be made a routine practice?"

There is no doubt that tuberculosis can be diagnosed earlier by x-ray than by any other method, In Dade County, Florida, from Oct. 15, 1947, to Dec. 19, 1947, about 65 days, 100,124 70 mm. chest films were taken. Disease was found in 1,456, or in about 1.5 per cent. Dr. Bickerstaff found pathologic conditions in 4 per cent of his 3,576 cases. It must be borne in mind, however, that nearly half of his cases were selected cases. In Dade County definite or suspicious tuberculosis was found in 1,025 cases or slightly more than 1 per cent. Follow-up on 887 cases showed definite and suspected tuberculosis in 606 cases, or 69 per cent, and 281 cases not tuberculosis, or 31 per cent. Tuberculosis was found in 0.7 of 1 per cent of total patients x-rayed. Dr. Bickerstaff found 1.6 per cent but bear in mind nearly half of his cases were selected. Hence one is led to believe that tuberculosis in pregnancy occurs in about the same ratio as in the population in general.

In Table V he shows that out of 37 women with tuberculosis, 28 were already known to have the disease, leaving only 9 out of 3,576 or about 0.25 of 1 per cent who were actually found by this survey—the majority of whom might well have been from the selected group. I wish he had shown the number found in this selected group. Of the 9 found, only 3 cases were shown as active.

From this study an opinion could be expressed as follows:

1. Routine prenatal chest x-ray is desirable but is impractical economically.

2. About 1 per cent of all people x-rayed in general survey have tuberculosis.

3. Known tuberculous individuals should practice contraception.

4. Suspected tuberculous persons who become pregnant should be studied closely by x-ray, both ante partum and post partum.

THE MORPHOLOGICAL CHANGES IN THE CERVIX DURING PREGNANCY, INCLUDING INTRAEPITHELIAL CARCINOMA*

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THE morphological changes in the pregnant cervix, especially those in the glandular epithelium, have been rather extensively described by Vallerini, Stieve, Hofbauer, Levy, and others. More recently, McIlrath has described the pregnancy changes in the cervical glands especially as they relate to infection, while Sheets has reported on the histological findings in the cervix at delivery.

The above studies are not altogether complete in that they deal only with either the cervical glands or the epithelium, and do not follow the changes in the cervix throughout pregnancy and the puerperium. Furthermore, the problem of intraepithelial carcinoma arises. Although it is accepted that this is the earliest malignant change in the nonpregnant cervix which can be recognized, competent obstetrical and gynecological pathologists have been hesitant to make this diagnosis during pregnancy. In view of the above-mentioned facts, it seemed desirable to perform cervical biopsies on a large number of pregnant women during the prenatal period, at delivery, and in the puerperium, in order that a systematic study of both the glandular and stratified squamous epithelial changes could be carried out. In addition, it was planned to give special attention to the hyperplastic changes of the cervical epithelium with particular reference to their relationship to carcinoma.

TABLE I. THE INCIDENCE OF VARIOUS LESIONS IN 87 BIOPSIES OF PREGNANT CERVICES OBTAINED FROM 1938 TO 1948

	NUMBER	PER CENT
Cervicitis	84	97
Squamous metaplasia	25	29
No squamous epithelium	23	27
Polyp	18	21
Decidual reaction	17	20
Hyperactive epithelium	10	15*
Condylomata acuminata	8	9
Epidermoid carcinoma	2	2
Total Cases	87	100

*Corrected for 23 cases showing no squamous epithelium.

The taking of cervical biopsies during pregnancy has been believed to be attended with danger of hemorrhage, infection, abortion, and the onset of premature labor. For these reasons, relatively few cervical biopsies have been obtained in this clinic during the past ten years. Furthermore, all biopsies which were previously obtained were taken because of definite gross abnormalities of the cervix. The diagnoses on these biopsies appear in Table I.

With this material as a background, the study upon which this paper is based was projected. Patients were chosen at random from the Prenatal Clinic of the Johns Hopkins Hospital, the only criterion being that the cervix should appear grossly normal. Biopsies were taken with a punch biopsy clamp at various intervals during the prenatal period as shown in Table II. Two hundred eighty-six patients were biopsied prenatally, 32 of whom had two prenatal biopsies. Of these, 214 were biopsied at delivery and 220 were subjected to biopsy from four to eight weeks post partum. In all, 752 biopsies were taken. These were fixed immediately in 10 per cent neutral formalin, imbedded in paraffin, sectioned, and stained with hematoxylin and eosin. In addition, the first 445 biopsies were stained with para-iodo-acetic acid in order to determine their glycogen content and distribution. Each microscopic section was examined by at least three individuals and no diagnosis was recorded unless all three concurred. To check the accuracy of the pathological interpretation, old sections on which a diagnosis had been previously made were periodically placed among the new specimens to be examined. In all these, the diagnosis remained essentially the same on the second and third review. It was, therefore, felt that the pathological interpretation was standardized. Table III shows the distribution of these patients by race, age, and parity.

TABLE II.   DISTRIBUTION OF BIOPSIES PER PATIENT AND TIME OF BIOPSY

TIME OF BIOPSY	NUMBER OF PATIENTS	TOTAL NUMBER OF BIOPSIES
Prenatal only	43	43
Prenatal and delivery	19	38
Prenatal, delivery, and post partum	168	504
Prenatal and post partum	24	48
Two prenatal, delivery, and post partum	27	108
Two prenatal and post partum	1	3
Two prenatal only	4	8
Total	286	752

TABLE III.   DISTRIBUTION OF PATIENTS AS TO RACE, PARITY, AND AGE

AGE IN YEARS	WHITE								NEGRO								TOTAL
	0	I	II	III	IV	V	VI+	TOTAL	0	I	II	III	IV	V	VI+	TOTAL	
14	1							1	12							12	14
15-19	9	6						15	35	15	2	1				53	68
20-24	11	10	5	2				28	31	26	9	5				71	99
25-29	4	9	3	1	1	1		19	12	7	8	9	1	1	2	40	59
30-34			4	1	1			6	7	3	5	3	2			20	26
35-39			1	1	2			4	3	2	1	1	1	1	1	10	14
40							1	1		1		2		1		4	5
Unknown												1			1	2	2
Total	25	25	13	5	4	1	1	74	100	54	25	22	4	3	4	212	286

It is to be regretted that all the patients biopsied during the prenatal period could not also have been examined at delivery and during the puerperium. However, some of these patients were delivered elsewhere and a few did not complete their prenatal course in the Obstetrical Dispensary. In addition, 10 per cent of the delivered patients did not return for postpartum examination. The fear of serious hemorrhage from prenatal biopsies was unfounded. Each biopsy site was cauterized with a silver nitrate stick and occasionally a vaginal pack was inserted for thirty minutes. All patients were told to return to the Accident Room if vaginal bleeding or spotting occurred. Only one patient bled so vigorously that admission was necessary. Nevertheless, approximately one-fifth of the patients returned within twenty-four hours because of bleeding but either reassurance or additional cauterization sufficed to meet the situation. Biopsy at delivery and post partum caused no difficulty. There were no infections in any of these patients. Only nine patients aborted and all but one of these abortions occurred more than fourteen days after the biopsy was obtained. This abortion rate is less than the clinic average of 10 per cent. There were twenty-one premature deliveries in the series; all these infants survived and the premature rate is less than the clinic average. It would thus appear that the fears previously entertained regarding the danger of cervical biopsy in pregnancy were unfounded.
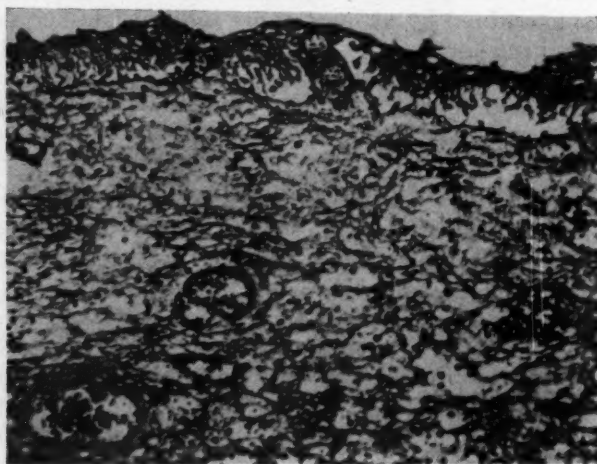
Fig. 1.—Extreme edema, vascularity, and thinning of the stratified squamous epithelium found in biopsies taken at delivery.

The morphological changes in the cervix will be discussed under three headings, namely, stroma, glands, and epithelium.

Under the influence of pregnancy the stroma of the cervix is modified in four ways: (1) An increased vascularity develops which is directly proportional to the duration of pregnancy until at parturition the stroma appears almost angiomatous. (2) An increasing edema occurs which usually accompanies this vascular change and at delivery the stroma swells and thins out the overlying stratified squamous epithelium as shown in Figs. 1 and 2. At delivery, there is also an infiltration of red blood cells. The edema and vascularity begin to disappear within twenty-four hours after parturition and in ninety-six hours the stroma presents an almost normal nonpregnant appearance.

(3) Cervicitis in this series was prominent throughout pregnancy and the postpartum period as seen in Table IV. Over 50 per cent of all biopsies show this finding.

TABLE IV. INCIDENCE OF VARIOUS PATHOLOGICAL LESIONS IN THE PRENATAL, DELIVERY, AND POSTPARTUM INTERVALS

	FIRST PRENATAL	SECOND PRENATAL	DELIVERY	POST PARTUM	TOTAL
Total biopsies	286	32	214	220	752
Normal	33	4	33	61	131
No squamous epithelium	1	0	10	7	18
No glandular epithelium	101	8	56	45	210
Cervicitis	138	18	118	121	395
Decidua	27	3	45	8	83
Epidermization	37	4	8	2	51

(4) The diagnosis of decidual reaction is somewhat difficult and the figures cited by previous authors show considerable variation. The difficulty stems from the fact that occasionally swollen and edematous stromal cells have a decidua-like appearance. However, the checking of these biopsies by a number of different observers should give a reasonably accurate incidence of this change. When true decidua occurs in the stroma there is no mistaking this diagnosis (Fig. 2). The incidence of this reaction varies with the duration of pregnancy and disappears rapidly in the postpartum period. Table V shows an incidence of 10.4 per cent prenatally, 21 per cent at delivery, and 3.1 per cent in the postpartum period. The earliest decidual change was found at the sixteenth week of pregnancy.
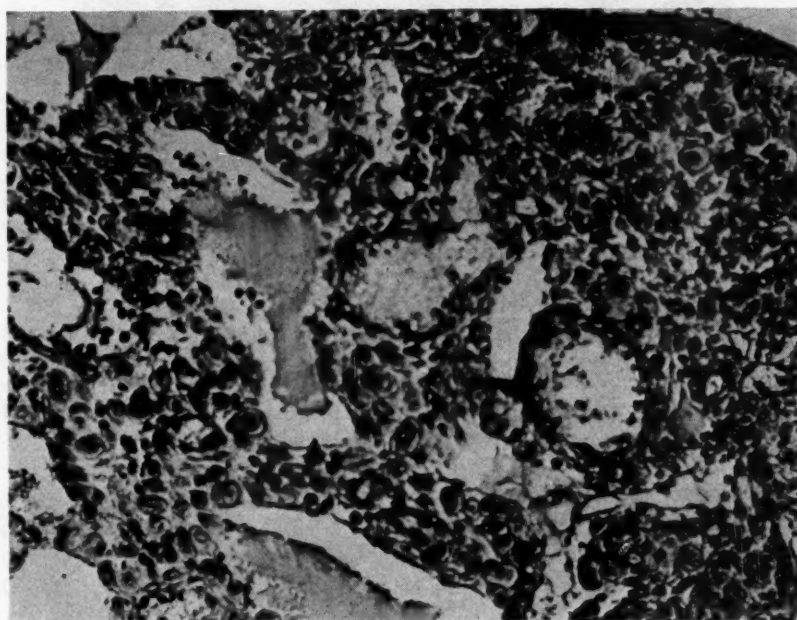
Fig. 2.—Decidua-like reaction occurring in the cervical stroma.

There are four changes in the glandular epithelium of the cervix directly related to pregnancy, as follows:

1. Glandular hyperplasia (Fig. 3). This was well described by Stieve. There is a great increase in the number of glands until the entire stroma of the cervical canal seems to be filled with glandular tissue.

2. Hyperplasia of the glandular epithelium. There is an increase in the number of cells lining the glands so that instead of there being one layer there appear to be three or more cell layers.

3. Adenomatous hyperplasia (Fig. 4). This change has been termed by some "glands within glands." It consists of the formation of multiple small gland spaces within the larger glands. These are lined with columnar or flattened epithelium. This latter change has been described by McIlrath. A similar change has been noted in the glands of the prostate by Moore.
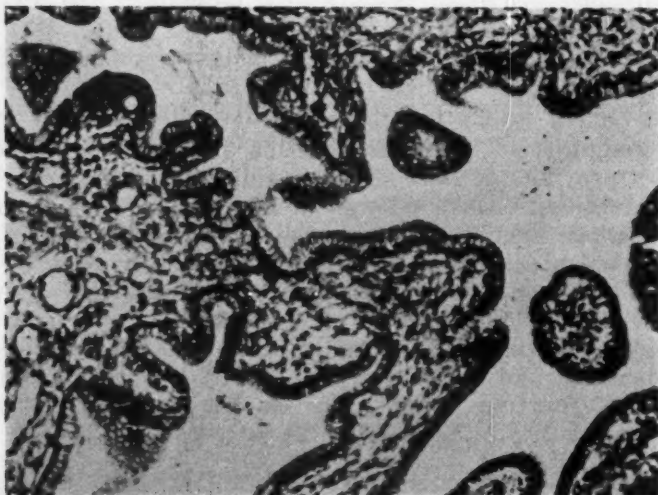
Fig. 3.—Glandular hyperplasia. Merely a great increase in the number of glands.
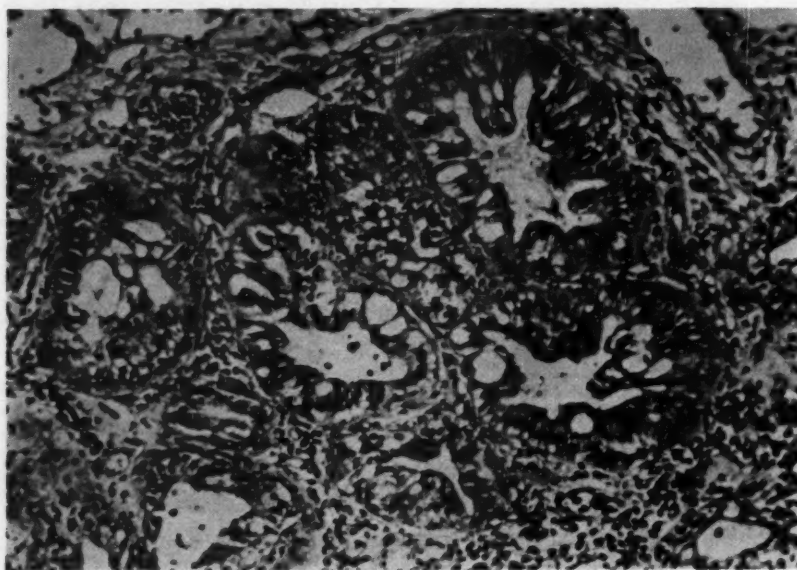
Fig. 4.—Adenomatous hyperplasia. Formation of "glands within glands." This reveals both the columnar and flattened epithelium that lines these glands.

The distribution of these changes is shown in Table VI. Thirty-six out of 209 prenatal biopsies with glandular epithelium, or 17.1 per cent, have some change in the glandular morphology, as compared with 14.8 per cent at delivery and 9.1 per cent in the postpartum period. The difference between the prenatal and delivery changes is not statistically significant but there is a real

decrease in the incidence of these findings during the puerperium. This would seem to indicate that the glands show a definite reaction to the pregnant state.

4. Epidermization (Fig. 10). The stratified squamous epithelium grows beneath the columnar epithelium of the endocervical glands or replaces it in 14.3 per cent prenatally, compared to 3.5 per cent at delivery, and 0.9 per cent in the postpartum interval. This is shown in Table IV.

TABLE V. DISTRIBUTION OF PATIENTS WITH STROMAL DECIDUAL REACTION BY AGE AND PARITY

AGE IN YEARS	318 BIOPSIES PRENATALLY							214 BIOPSIES AT DELIVERY											TOTAL
	PARITY							PARITY											
	0	I	II	III	IV	V	TOTAL	0	I	II	III	IV	V	VI	VII	VIII	IX	TOTAL	
14	3+						3	3										3	6
15-19	4	3					7	10	2									12	19
20-24	5+	5					10	3	7	3	2		1					16	26
25-29	2	2+	1				5	2	2	1	1							6	11
30-34			1	1			2		2		1							3	5
35-39			1		1		2		1		1							3	5
40				1			1								1		1	1	2
Unknown									1									1	1
Total	14	10	3	2	1		30	18	9	8	4	3	1		1		1	45	75

TABLE VI. DISTRIBUTION OF GLANDULAR CHANGES IN THE PRENATAL, DELIVERY, AND POSTPARTUM INTERVALS

	FIRST PRENATAL	SECOND PRENATAL	DELIVERY	POST PARTUM	TOTAL
Glandular hyperplasia	17	5	4	10	36
Adenomatous hyperplasia	11	2	13	3	29
Hyperplasia, glandular epithelium	0	1	6	3	10
Total	28	8	23	16	75
Total biopsies with glandular epithelium	185	24	158	175	542

The increase in edema and vascularity previously noted in the stroma is likewise found in the stratified squamous epithelium during pregnancy. The increase in the vascularity of the cervix is merely a reflection of the tremendous circulatory change occurring in the genital tract during this period. The circular arterioles of the epithelium become more numerous and larger. Occasionally thrombosis occurs. Sometimes this thrombus liquefies with the formation of small, endothelium-lined cysts as shown in Fig. 8. This great increase in vascularity of the epithelium gives the cervix its blue appearance during pregnancy and easily accounts for the increase in cervical bleeding following trauma.

The question of whether hyperactivity of the basal layer of the epithelium occurs normally in pregnancy is of great importance for this change is intimately related to the occurrence of intraepithelial carcinoma. Unfortunately, the incidence of this change in normal cervices in nonpregnant individuals is not known. For the purpose of this paper hyperactivity of the basal cells was divided into three grades as follows:

Grade I (Fig. 5).—Slight hyperactivity of the basal cells consists of an increase in the number of these cells from the usual thickness of one to two to six to seven layers. There is a corresponding increase in mitotic figures and anaplasia of the cells but these cells never lose their polarity and never invade the basement membrane.

Grade II (Fig. 6).—In this figure there is an increase in the basal cells on the right side of the photograph so that they occupy one-half the thickness of the stratified squamous epithelium. This is well shown in Figure 6 for it contrasts with a normal area on the left and a rete peg in the center with the area of hyperactivity on the right.

Grade III (Fig. 7).—This is the most severe type of basal-cell hyperactivity. Here the basal cells occupy the full thickness of the stratified squamous epithelium. There is hyperchromatosis of the nuclei with many mitotic figures present. Although the cells are anaplastic they do maintain their polarity and invasion of the basement membrane does not occur.

Hyperactivity of the basal layer of the epithelium was found in 14.7 per cent of all prenatal biopsies (Table IX). There was no significant correlation between age and parity in the occurrence of this finding as shown in Table VII. However, Table VIII reveals a slight tendency toward a gradual increase in the incidence of hyperactivity up to the twenty-eighth week of pregnancy. There is rapid diminution in the incidence of this condition after delivery.

TABLE VII. DISTRIBUTION OF PATIENTS WITH BASAL CELL HYPERACTIVITY BY AGE AND PARITY

AGE IN YEARS	318 BIOPSIES PRENATAL PARITY							214 BIOPSIES AT DELIVERY PARITY							220 BIOPSIES POST PARTUM PARITY							TOTAL
	0	I	II	III	IV	V	TOTAL	0	I	II	III	IV	V	TOTAL	0	I	II	III	IV	V	TOTAL	
14	4+						4	1						1								5
15-19	12	1	1	2			16	5	1					6	4						4	26
20-24	8	4	1+				13	4	4	1				9	3	4	1				8	30
25-29	4+	4+	1		1		10	1		1	1		1	4			1				1	15
30-34		1	2+	1			4															4
35-39									1	1				2					1		1	3
40																						
Total	28	10	5	3	1		47	11	6	3	1		1	22	7	4	1	1	1		14	83

+Indicates 1 hyperactive biopsy from second prenatal biopsy, 5 in 32 hyperactive.

TABLE VIII. DISTRIBUTION OF PATIENTS WITH BASAL-CELL HYPERACTIVITY BY RACE AND DURATION OF PREGNANCY

RACE	WEEKS PREGNANT	0-4	5-8	9-12	16-18	17-20	21-24	25-28	29-32	33-36	37-40	TOTAL
Negro	Total cases	–	7	6	30	35*	40*	47	41	26*	2	234
	Total hyperactivity	–	1	1	7	7	4	7	5	2	–	34
White	Total cases	–	2	3	7	15	18	14*	14	11	–	84
	Total Hyperactivity	–	0	0	1	2	1	4	4	1	–	13
White and Negro	Total cases	–	9	9	37	50	58	61	55	37	2	318
	Total hyperactivity	–	1	1	8	9	5	11	9	3	0	47

*Includes 32 second prenatal biopsies, 5 with hyperactivity.

TABLE IX. DISTRIBUTION OF BIOPSIES AND INCIDENCE OF BASAL CELL HYPERACTIVITY IN THE PRENATAL, DELIVERY AND POSTPARTUM INTERVALS

	FIRST PRENATAL	SECOND PRENATAL	DELIVERY	POST PARTUM
Total biopsies	286	32	214	220
Total hyperactive	42	5	22	14
% hyperactive	14.5%	15.5%	10.2%	6.3%
	14.7%			

Fig. 5.—Basal cell hyperactivity, Grade I. Hyperactivity noticed in only a few of the basal cells.
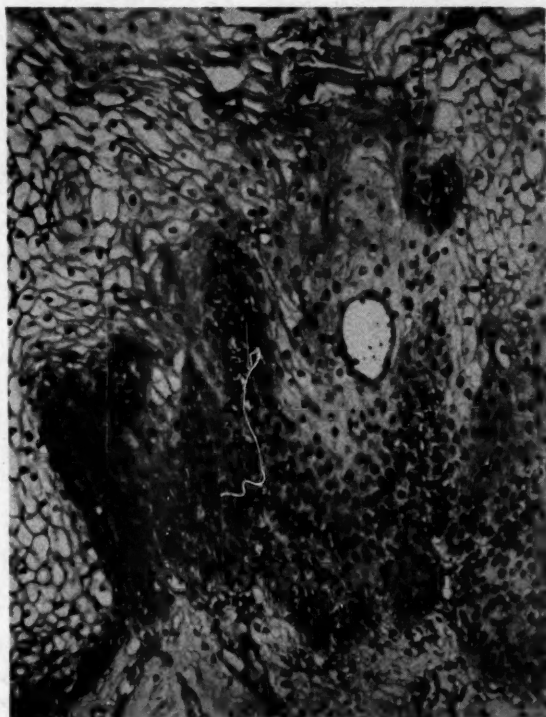

Fig. 6.—Basal cell hyperactivity, Grade II. Note the contrasting normal area on the left with a rete peg in the center of the photograph.

Table X shows the distribution of the various grades of activity by time of biopsy. If the questionable group, that is Grade I, is eliminated, the change between prenatal, delivery, and postpartum incidence is striking with a 9.8 per cent occurrence prenatally, 4.1 per cent at delivery, and 1.8 per cent post partum.

TABLE X. INCIDENCE OF THE THREE GRADES OF BASAL-CELL HYPERACTIVITY
BY TIME OF BIOPSY

	FIRST PRENATAL	SECOND PRENATAL	DELIVERY	POST PARTUM	TOTAL
Basal-cell hyperactivity I	17	1	13	10	41
Basal-cell hyperactivity II	14	3	8	4	29
Basal-cell hyperactivity III	11	1	1	0	13
Total	42	5	22	14	83

Hyperactivity of the basal layer was found in patients as young as 13 years and as early as the eighth week in pregnancy. Although occasionally found in the sixth postpartum week, 85 per cent of those patients with basal-cell hyperactivity were normal by the fourth postpartum week.
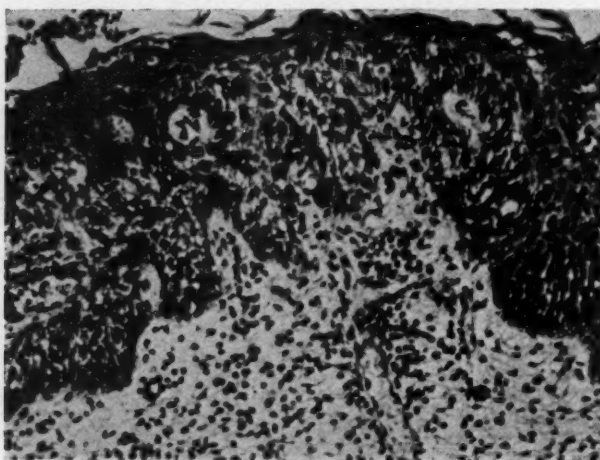
Fig. 7.—Basal cell hyperactivity, Grade III. Hyperchromatosis, anaplasia, mitosis are present, but basement membranes invasion and loss of polarity have not occurred.

A total of 71 patients having 83 biopsies showing hyperactivity gave a patient incidence of 24.8 per cent. If the postpartum biopsies are eliminated, then 19.9 per cent of all patients had hyperplasia of the basal epithelium either prenatally or at delivery.

The dividing line between hyperactivity of the basal layer and intra-epithelial carcinoma is a fine one and requires expert judgment and prolonged experience. In the present study there were two instances of what would be called in nonpregnant women "intraepithelial carcinoma." In addition, in a preliminary study conducted the year before there were three examples of this finding. These slides have been checked by numerous competent pathologists and there is general agreement as to the diagnosis. Fig. 9 is a typical example of this lesion. There is clear demarcation between the normal and the abnormal tissue. There is pronounced hyperactivity of the basal cells extending the full width of the stratified squamous epithelium. Hyperchromatosis of the nuclei with many mitotic figures and rather marked ana-

plasia of the cells is present. There is a distinct loss of polarity of the cells with a questionable invasion of the basement membrane. The history of these five cases is given in detail.
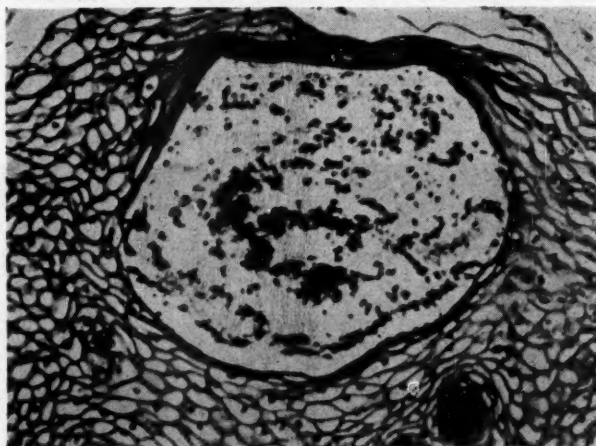
Fig. 8.—Small endothelium-lined cyst found in the squamous epithelium, resulting from liquefaction of a small thrombus.
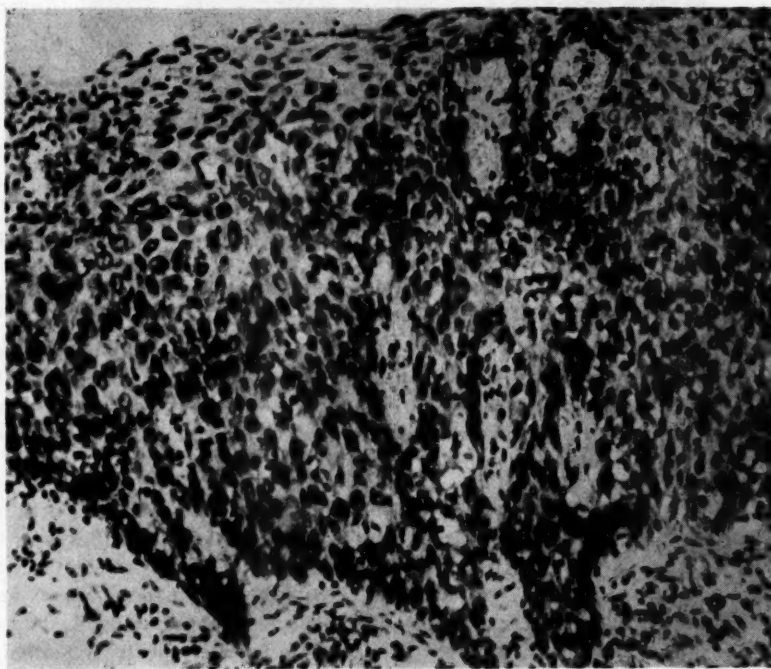
Fig. 9.—Typical lesion in the pregnant cervix which exactly simulates intraepithelial carcinoma in the nonpregnant woman.

CASE 1.—D. C., a 27-year-old Negro woman, para iii-o-o-iii-o, was first seen in the Gynecological Dispensary in the second month of her pregnancy. Grossly the patient had an inflamed cervix with marked erosion. A cervical biopsy was reported as intraepithelial carcinoma. During the next six weeks, four additional biopsies of the cervix revealed only epidermization of the endocervical glands and basal-cell hyperactivity of the squamous epithe-

lium. Spontaneous abortion occurred in the patient's fourth gestational month. Three additional cervical biopsies obtained during the six-week postpartum period following her abortion revealed only chronic cervicitis and epidermization.

CASE 2.—W. H., a 22-year-old Negro woman, para ii, was examined in the third month of her third pregnancy. Grossly, the cervix was inflamed and eroded. A cervical biopsy was reported as early epidermoid carcinoma. Two weeks later spontaneous abortion occurred. Follow-up biopsy at six weeks, six months, and twenty months, showed only normal stratified squamous epithelium.
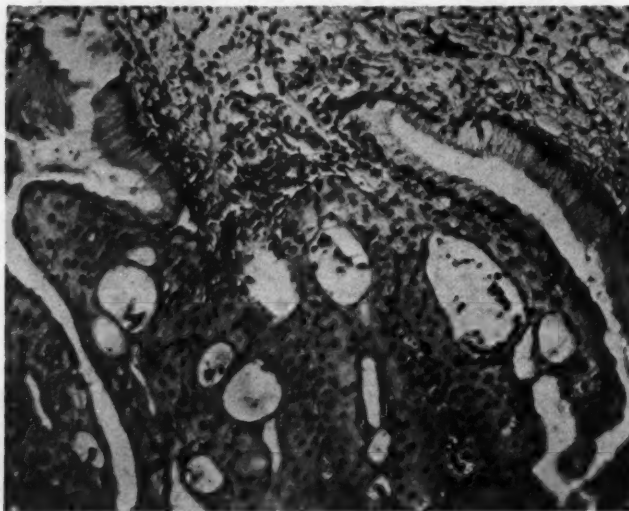
Fig. 10.—Epidermization. The stratified squamous epithelium has grown beneath the glandular epithelium.

CASE 3.—N. I., a 38-year-old white, para iii, was examined in the third month of her fifth pregnancy. A suspicious lesion of the cervix was biopsied. In view of the two previous cases this was reported as basal-cell hyperactivity of the squamous epithelium and a repeat biopsy was requested. This was obtained and reported as epidermoid carcinoma. Near term the patient was delivered by means of a cesarean section. A biopsy obtained eleven days post partum was histologically benign. The patient was followed in the Out-Patient Dispensary and at six weeks cervical curettage and conization were done with a scalpel. Pathological sections revealed a normal stratified squamous epithelium. This patient was also followed for twenty months and biopsies remained normal.

CASE 4.—E. H., a 24-year-old Negro woman, para iii, was in her fourth pregnancy. Grossly, the cervix was normal. A cervical biopsy was obtained in the twenty-fourth week of pregnancy. This was diagnosed as intraepithelial carcinoma. The patient delivered in her thirty-fourth week of pregnancy by means of cesarean section because of an abruptio placentae. The patient's postpartum biopsy was reported as normal and the patient has now been followed for nine months and her cervical biopsies are repeatedly normal.

CASE 5.—G. P., a 33-year-old, white, para ii, was in her third pregnancy. The patient had a grossly normal cervix. She was biopsied in her twenty-eighth week of pregnancy. This biopsy was reported as intraepithelial carcinoma. The patient delivered a normal infant per vaginam at term. Her postpartum biopsies at that time were normal. This patient has been followed for eight months and the cervical biopsies are repeatedly normal.

From the above histories it will be seen that none of these patients was treated for carcinoma, but all have been followed meticulously: two for

twenty months, two for eight months, and one for one and one-half months. During this period multiple biopsies were taken, all of which were normal.

Conclusions

1. The gestational changes in the human cervical stroma consist of edema, increased vascularity, a high frequency of leucocytic infiltration and a 10 to 20 per cent incidence of decidual reaction.

2. In the glands, pregnancy causes hyperplasia of the epithelium, hyperplasia of the glands, and adenomatous hyperplasia. In addition, epidermization occurs in about 14 per cent of cases.

3. There is an increased vascularity and edema of the epithelium. Basalcell hyperactivity occurs in 19 per cent of all pregnant individuals. Whether this is an increased incidence of this condition over the incidence in the nonpregnant woman cannot be stated at this time. There were at least five instances of a type of alteration which in nonpregnant women would be called "intra-epithelial carcinoma." These occurred during a two-year period in which 4,849 deliveries occurred. This gives an incidence of 0.1 per cent which is double the usually cited instance. Of great interest is the fact that, although these patients were allowed to go through their pregnancy, all appeared normal at postpartum biopsies.

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TRANSVERSE PRESENTATION OF THE FETUS

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TRANSVERSE presentation is one of the less frequent complications of pregnancy, but it is an important cause of morbidity and mortality resulting from delivery.

Prior to 1900 most of the literature on transverse presentation originated in Germany and it was limited mostly to a discussion of the time at which an internal version should be done. Cesarean section was rarely used and destructive operations were frequently performed. Eastman, in 1932, was one of the first Americans to present an analysis of a large series of cases with transverse presentations. Other papers on this subject were published by Paine, Torpin, Novey and Schneider, Cole and Delaney, Ware, Stevenson, and Johnson.

Material

In the Medical College of Virginia Hospitals, since 1933, 65 cases of true transverse presentation have occurred in 27,249 deliveries, an incidence of 0.24 per cent, or 1 in 419 deliveries. All cases of twins have been omitted and all cases in which the infant weighed less than 1,500 grams were also omitted. One case in which an external version was done during labor is included because the transverse presentation during labor was confirmed by x-ray studies.

A review of the maternal deaths and morbidity occurring on the obstetrical service of the Medical College of Virginia Hospitals during this period of sixteen years reveals the dangers associated with transverse presentation during labor.

This paper is presented with the hope that other physicians may profit by our experience and mistakes. In the sixty-five cases with transverse presentation there were six maternal deaths, a maternal mortality rate of 9.2 per cent. In the eight years since 1941 there have been 20,755 births in the Medical College Hospitals and 26 patients with transverse presentations have been delivered with no maternal death associated with this complication.

The results obtained in treating any group of patients will depend on the judgment and skill of the attending physicians and the condition of the patients when the physicians are first consulted. The Medical College Hospitals admit a relatively high percentage of abnormal and neglected obstetrical cases from the City of Richmond and a large surrounding territory. Prior to the opening of the new hospital in 1942 all uncomplicated deliveries of clinic patients were performed at home, and very few private patients were admitted to the hospitals.

An analysis of the cases shows approximately 14 per cent of the patients were less than 20 years of age, 43 per cent were between 20 and 30 years, and 43 per cent were over 30 years of age.

In Table I the cases have been divided into three groups according to years with 22 cases in each of the first five-year periods, and 21 cases in the six-year period commencing in 1944. During these last six years 17,369 deliveries occurred, but only 21 transverse presentations were encountered.

TABLE I. OCCURRENCE IN REFERENCE TO YEARS

YEARS	NO. OF CASES	PER CENT
1934-1938 (5 years)	22	33.8
1939-1943 (5 years)	22	33.8
1944-1949 (6 years)	21	32.3
Total 1934-1949 (16 years)	65	99.9

The decrease in the incidence of transverse presentation during the last six years of this study can probably be explained by the increase in the admission of normal obstetrical patients to the hospitals. However, it is probable that many of the early cases were not true primary transverse presentations and were admitted to the hospitals after someone had attempted an internal podalic version on the patient at home.

An attempt to determine the etiological factors responsible for transverse presentation in this group did not reveal anything of importance. In most textbooks contracted pelvis is given as the chief cause of transverse presentation, but it was diagnosed in only 4.6 per cent of our cases. Placenta previa was found in 7.7 per cent of the patients.

Stevenson, in a recent paper, reported a study of 52 cases of transverse presentation at the Boston Lying-in Hospital. All of his cases were studied during the last ten weeks of pregnancy. In 63.5 per cent of his cases the fetus had changed to a longitudinal presentation before the onset of labor or at the time of delivery. Stevenson concluded "that the position of the placenta, in situ in the near-term uterus, has a definite influencing effect upon the presentation of the fetus in an appreciable proportion of cases." He thinks transverse presentation of the fetus often results from implantation of the placenta in the fundus or lower segment of the uterus, particularly in multiparas.

TABLE II. INCIDENCE IN REFERENCE TO DURATION OF PREGNANCY

DURATION OF PREGNANCY	NO. OF CASES	PER CENT
Less than 28 weeks	4	6.2
28-32 weeks	4	6.2
33-36 weeks	15	23.1
37-39 weeks	15	23.1
40 weeks and over	27	41.5
Total	65	100.0

Abnormal presentations occur more frequently in premature labors than in term pregnancies. Table II shows that 6.2 per cent of our patients were less than 28 weeks pregnant, 29.3 per cent were between 28 and 36 weeks, 23.1 per cent were between 36 and 39 weeks, and 41.5 per cent were more than 39 weeks pregnant.

Twenty per cent of the patients were primiparas and 80 per cent had one or more babies. The incidence in reference to parity is shown in Table III.

TABLE III. INCIDENCE IN REFERENCE TO PARITY

PARITY	NO. OF CASES	PER CENT
0	13	20.0
i	11	16.9
ii	14	21.5
iii or iv	12	18.5
v or more	15	23.1
Total	65	100.0

The arm prolapsed in 45 per cent of the cases and the other complications are also recorded in Table IV.

TABLE IV. COMPLICATIONS OF LABOR

COMPLICATION	NO. OF CASES	PER CENT
Prolapsed arm and cord	13	20.0
Prolapsed arm, foot, and cord	1	1.5
Prolapsed cord	3	4.6
Prolapsed arm	16	24.6
Toxemia or hypertension	8	12.3

Table V shows the type of delivery and the fetal mortality (stillbirths and neonatal deaths) associated with each. The lowest gross fetal mortality occurred in the patients delivered by cesarean section. Three of the cesarean sections were done because of maternal indications and no fetal heart sounds were heard when these patients were admitted to the hospital. In 13 patients delivered by cesarean section, fetal heart sounds were heard on admission and 12 live babies were obtained, a corrected fetal mortality of 7.7 per cent in this group.

TABLE V. METHOD OF DELIVERY AND FETAL MORTALITY

METHOD OF DELIVERY	NUMBER OF CASES	PER CENT OF TOTAL TRANS- VERSE PRESEN- TATIONS	FETAL MORTALITY		PER CENT
Cesarean section	16	24.6	4		25.0
Not delivered	1	1.5	1		100.0
Vaginal delivery	48	73.8	43		89.6
External version spon- taneous	1	1.5		1	100.0
Spontaneous evolution	3	4.6		3	100.0
Braxton Hicks version	11	16.9		10	90.9
Internal version and extraction	33	50.8		29	87.9
	65	100.0	48		73.8

Internal podalic version and breech extraction have, in the past, been considered by some as the method of choice in delivering a patient with transverse presentation. Fifty per cent of the patients in this series were delivered by version and extraction with a fetal mortality rate of 87.9 per cent. The fetal mortality rate has been reduced 25 per cent during the past six years, while delivery by cesarean section has increased to 57 per cent.

In 17 patients the cord prolapsed and 16 babies were stillborn, 94.1 per cent of this group.

TABLE VI. FETAL MORTALITY IN REFERENCE TO YEARS

YEARS	NO. OF CASES	FETAL DEATHS	PER CENT
1934-38 (5 years)	22	18	81.1
1939-43 (5 years)	22	18	81.1
1944-49 (6 years)	21	12	57.1
Total	65	48	73.8

The fetal mortality was high even when the duration of labor was short, and when the duration of labor was more than 24 hours the fetal mortality increased to 94.4 per cent.

Table VI shows the gross fetal mortality during the three periods of time included in this report. The 25 per cent reduction in fetal mortality during the past six years is encouraging.

The fetal mortality in collected reports is shown in Table VII. Eastman and Cole and Delaney did not deliver by cesarean section any patients with transverse presentations when the fetus was nonviable. In Johnson's cases and those reported by us, cesarean section was performed sometimes because of maternal indications even when the fetus had died in utero. In all of the collected reports, cesarean section gave the highest percentage of live babies.

TABLE VII. FETAL MORTALITY IN COLLECTED CASES. FETAL HEART HEARD ON ADMISSION

	VAGINAL DELIVERY			CESAREAN SECTION		
AUTHOR	NO. OF CASES	FETAL DEATHS	PER CENT	NO. OF CASES	FETAL DEATHS	PER CENT
Eastman	49	21	42.9	21	0	0.0
Cole and De- laney	28	5	17.9	30	0	0.0
Johnson	75	32	42.7	16	4	25.0
Garber and Ware	15	10	66.7	13	1	7.7
Total	167	68	40.7	80	5	6.3

Summary of Maternal Deaths

CASE 1.—Unit No. 17958 (1934). This patient, a 28-year-old Negro para ii, was referred to the hospital from the clinic because of a 36-week pregnancy, complicated by toxemia. After 5 days of conservative treatment labor was induced with a No. 4 Voorhees bag. After the bag was expelled the membranes were ruptured artificially and the cord prolapsed. Delivery was completed by version and extraction after a total labor of 6½ hours. Peritonitis and paralytic ileus followed and the patient died 20 days after delivery. *Comment:* With the use of blood and the antibiotics this patient probably would have survived.

CASE 2.—Unit No. 21125 (1934). This patient, a 35-year-old white para iv, was admitted to the hospital 16 hours after the onset of labor with an arm prolapsed. Delivery had been attempted at home. It was thought that the patient had a ruptured uterus. Version and extraction were done and followed by hysterectomy. The patient failed to improve and died from shock. *Comment:* Massive blood transfusions and delivery by cesarean section followed by hysterectomy probably would have prevented this death.

CASE 3.—Unit No. 33355 (1936). This patient, a 25-year-old Negro para ii, was referred to the hospital because of a prolapsed cord. Membranes had been ruptured for 72 hours and an attempt at delivery had been made at home. A Braxton Hicks version was done followed by extraction 24 hours later. Moderate hemorrhage followed extraction and blood was not available. The patient died as a result of hemorrhage and shock. *Comment:* Massive blood transfusion would have been of great value.

CASE 4.—Unit No. 56076 (1938). This patient, a 29-year-old Negro para vi, was referred to the hospital because of a prolapsed arm of 6 hours' duration. Nitrous oxide, oxygen, and a small amount of ether were administered to facilitate examination. While the patient was being examined, her respiration became shallow and labored. All attempts to revive her failed. Autopsy was performed but death could not be explained. *Comment:* A competent anesthetist might have prevented this death.

CASE 5.—Unit No. 47608 (1939). This patient, a 26-year-old Negro para iii, was admitted to the hospital because of prolapsed cord and arm. Delivery had been attempted at home. After admission she was delivered by version and extraction. A septic course

followed with pelvic cellulitis, abscess formation, and peritonitis. She died 59 days after admission. *Comment*: Probably transfusions with whole blood and antibiotics would have saved this patient.

CASE 6.—Unit No. 78593 (1941). A 22-year-old Negro, para iv, was a clinic patient referred to the hospital by the home delivery service because of chills, fever, transverse presentation, and ruptured membranes. She was delivered by version and extraction 16 hours after admission. The placenta did not separate. Four and one-half hours after delivery she commenced having excessive vaginal bleeding and her blood pressure dropped. The placenta was removed manually and a ruptured uterus was discovered. The patient died before surgery could be started. *Comment*: Manual removal of the placenta immediately following delivery and exploration of the uterus would have indicated the necessity of immediate surgery.

Table VIII shows a decrease in maternal mortality associated with transverse presentation of the fetus. There was no maternal death in the last six-year period. Actually the last maternal death in our series occurred in 1941.

TABLE VIII. MATERNAL MORTALITY AND MORBIDITY

YEAR	NO. OF CASES	DEATHS	PER CENT	MORBID	PER CENT
1934-38 (5 years)	22	4	18.2	12	54.6
1939-43 (5 years)	22	2	9.1	10	45.5
1944-49 (6 years)	21	0	0	7	33.3
Total	65	6	9.2	29	44.6

In the first five-year period of this report only one cesarean section was performed in 22 cases, and in the last six years twelve patients were delivered by cesarean section in a group of 21 transverse presentations. We think the increasing use of cesarean section in the management of this complication has reduced our maternal mortality and increased the number of fetal live births.

The presence of a transverse presentation in the last trimester of pregnancy necessitates close observation of the patient. Fortunately most transverse presentations convert spontaneously to vertex or breech presentations before the onset of labor. The persistence of a transverse presentation until near term often indicates the presence of some abnormality in the bony pelvis or the soft tissues of the mother, or a fetal abnormality. X-ray studies are indicated whenever a transverse presentation is suspected.

Treatment

Abdominal palpation during the last six weeks of pregnancy should be a routine procedure in prenatal care. External cephalic version should be attempted on all women with transverse presentations during the last month of pregnancy unless it is contraindicated or impossible. After the membranes have ruptured or labor has commenced the dangers associated with external version are definitely increased.

The membranes should be kept intact until the patient with a transverse presentation is ready for delivery. Premature rupture of the membranes increases both maternal and fetal mortality.

A Braxton Hicks version may sometimes be indicated if the fetus is dead, the pelvis ample, the cervix 2 or more cm. dilated, and the uterus relaxed.

If the patient is first seen after the cervix has completely dilated and the pelvis is normal, membranes intact, and uterus relaxed, we usually attempt delivery by internal podalic version and breech extraction.

Rupture of the uterus is a dangerous and frequent complication in neglected transverse presentation.

After vaginal delivery of a patient with transverse presentation an intrauterine examinaiton should be done to rule out rupture of the uterus.

The more frequent early use of cesarean section, particularly if the membranes have been ruptured early and the cervix is long, firm, and undilated, will decrease fetal and maternal mortality associated with transverse presentation.

The free use of the antibiotics and sulfonamides in infected or potentially infected cases is indicated. Transfusions of whole blood should be used when indicated.

Summary

1. Sixty-five cases of true transverse presentation have been presented and analyzed.

2. Transverse presentation is a dangerous complication of labor.

3. Transverse presentation should be diagnosed before the onset of labor and corrected by external cephalic version whenever this procedure is possible.

4. The more frequent use of cesarean section in the treatment of transverse presentation has decreased maternal and fetal mortality associated with this complication in the Hospitals of the Medical College of Virginia.

5. The use of the antibiotics, sulfonamides, and transfusions of whole blood has been of value in treating the neglected cases.

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Discussion

DR. RUDOLPH W. HOLMES, Charlottesville, Va.—Our modern obstetric concepts and practice are fundamentally based upon the precepts of authorities of past generations. There may be no argument that the marvelous development of recent scientific contributions, particularly those applicable to obstetrics, should and must modify the teachings and practice of past generations. It is indubitably true that little has been contributed to the art of obstetrics in late years, for cesarean section has supplanted vaginal deliveries. I would most emphatically assert that no one in his senses would advocate that we should revert to those direful methods in vogue fifty years ago when the surgical obstetric era

began. The modern younger obstetricians are unaware of the stresses their forebears faced a few decades ago, e.g., the routine attendance of parturients in the home, even the performance of major obstetric operations therein. They have escaped the necessity of the frequent use of manual dilatation, high forceps, symphysiotomy, and pubiotomy. Furthermore they have escaped the constant fear that puerperal sepsis would supervene from the "slip-ups" in very inadequate asepsis.

However, certain precepts pertaining to operations might be reaffirmed today: first, that the determination of which operation should be elected was dependent upon two considerations, a valid indication and conditions which permit the operation to be done; second, that the diverse operations for delivery are not competitive, but are complementary.

In past decades it was the teaching that the obstetrician was subject to drastic censure if his cesarean produced a dead baby or a teratic fetus, a teaching emanating from Carl von Braun (circa 1860)—and that teaching prevailed before x-ray became a part of our armamentarium. Cesarean section pre-eminently was an operation for the conservation of the lives of mother and child.

The maternal mortality of cesarean in the hands of experts in ideally equipped operating rooms has almost reached the vanishing point: that does not hold true in many quarters throughout the country where the rate may be unconscionably high. I believe our teaching should be directed toward those who do not have the wide experience, and whose operative environments are inadequate.

That fetal life is not salvaged by sections is revealed by the study of the published statistics: commonly the fetal death rate is directly comparable to the rate for the clinical material as a whole; in some clinics it is evident that the operators give too little regard to the fact of antepartum fetal deaths. The rate may be double that obtaining for the total fetal mortality rate.

It would be wise to bear in mind that cesarean section is not a panacea for all obstetric complications and it must be recognized that obstetric operations still have a definite place as means of delivery. External version in the late weeks of pregnancy is invaluable in the correction of malpositions and presentations, and may commonly be consummated with surprising ease. When it fails in its purpose the operation is not at fault, but the failure is due to the conditions which preclude its execution. Likewise, the internal version is an ideal operation in its appropriate field, and, I believe, should be more frequently performed. The operation is a *safe* one for mother and child under appropriate conditions. When attempted after the membranes have been ruptured for a protracted period, and hard labor has thinned the lower segment to the verge of uterine rupture, it is prohibited; at best, the fetus should be living.

It may well be believed that embryotomy (craniotomy, decapitation, evisceration) on the dead fetus has lost caste in our specialty, but it should be replaced as a valid procedure when its conditions have been met. The aversion to bringing forth a mutilated fetus is only a mawkish sentiment. The performance of the operation on the living child is utterly irrelevant to the subject.

The exhibition of penicillin, the sulfonamides, etc., as a prophylactic in cesarean sections, and as a curative afterward, is equally invaluable in all obstetric procedures.

DR. PAIGE E. THORNHILL, Norfolk, Va.—I was glad to hear Dr. Garber speak of the importance of external version in the later weeks of pregnancy. Like breech presentation, the best treatment for transverse presentation is prevention.

I know that most of these cases in Dr. Ware's series were neglected emergencies, not seen until in labor, with membranes ruptured and cord down. For this type of case, their results are remarkably good.

Ordinarily, however, in private and clinic practice, all of us have the patient on the table every week, after the thirty-second week of pregnancy, for checking presentation, position, and engagement. We know what the presentation is; when in doubt, we call for x-ray.

In the later weeks of pregnancy, the same treatment is indicated for transverse presentation as for breech presentation, namely, external version, as outlined in my paper before this Society two years ago.

When repeated corrections fail, the patient should be rechecked for disproportion, pelvic tumor, or a low-implanted placenta.

Our aim should be never to allow a patient to go into active labor while the baby is lying transversely. If preventive measures have failed, the indication for an elective cesarean is clear.

Prenatal care, when patients are seen early enough, holds the answer.

DR. R. GORDON DOUGLAS, New York, N. Y.—By the exclusion of transverse presentation in multiple pregnancy and infants weighing less than 1,500 grams the authors have given us a true picture of this abnormality as encountered during labor. Their incidence of this complication during the last half of the period under consideration is approximately 1:800 premature and term labors compared to our reported incidence of approximately 1:600.

The authors found an explanation (contracted pelvis and placenta previa) in only 12.3 per cent of their patients. They implied, however, that many other cases, especially during the earlier years under review, were caused by attempted version prior to admission to the hospital. Stevenson has recently attributed great importance to multiparity and the location of the placenta in the fundal region or in the lower uterine segment as causative factors. The higher incidence of this complication in premature labor as compared to labor at term and an increased frequency of occurrence in parous patients is in conformity with previously reported experience.

The authors have shown conclusively, both from a maternal and fetal point of view, that definitely better results are obtained when the number of cesarean sections is increased. Conversely, one may also say from the data presented that the number of disastrous results is decreased by performing fewer versions and extractions. I am in complete accord with the essayists' statement that in at least one-half of the instances of this complication the best results are obtained when delivery is accomplished by section.

Version and extraction done under the conditions specified by the authors should be very safe but such a situation is seldom encountered in practice. Our experience at the New York Lying-In Hospital was reported by Cole and Delaney and is included by the authors in Table VII. It is noted that slightly more than one-half of our patients were delivered by cesarean section with no fetal mortality while in the vaginal deliveries we had a fetal mortality of 18 per cent.

The authors have raised a controversial point in performing cesarean section for a maternal indication in the presence of a dead fetus. While we have not had to perform the operation under such conditions I can visualize clearly that such an occasion might arise and if it did I would not hesitate to follow their suggestion.

DR. S. A. COSGROVE, Jersey City, N. J.—Dr. Holmes has given us a very interesting review of some of the phases of obstetric history. He apparently reverts back in his memory with some degree of nostalgia to the period when obstetricians were forced, through relative lack of safety in resorting to cesarean section, to handle the situations which Dr. Ware has been discussing by a variety of intrauterine manipulations from below. While I confess to sharing this nostalgia in some degree, and have resorted in my past experience to all the procedures to which Dr. Holmes has alluded, I very strongly believe that most of these procedures must be considered adsolescent. This attitude, and the use of cesarean section in those cases in which vaginal delivery cannot be carried out with the most facility, are, in my opinion, very desirable tendencies, salutary alike for the mother in that it saves her from the many severe hazards frequently attending difficult vaginal delivery, and certainly for the baby, for whom such difficulty is tremendously hazardous. I would commend Dr. Ware's entire treatment of the problem.

DR. WARE (Closing).—It is not easy to present a paper showing a high maternal and fetal mortality, and this may be the reason why only a few papers have been published on transverse presentation.

Dr. Holmes has stressed the importance of carniotomy and embryotomy in the management of transverse presentation. We recognize that a destructive operation may be the procedure of choice in the rare case of transverse presentation, but transverse presentations can be recognized early and treated promptly so that both mother and baby may survive.

We reported three cesarean sections done entirely in the interest of the mother. In all three of the patients the indication for operation was a ruptured or suspected rupture of the uterus. All three patients had been poorly managed before they entered the hospital.

Decapitation and embryotomy in the presence of a contraction ring and a tight uterus cannot be completed without considerable danger to the mother and of course death of the fetus.

A discussion of transverse presentation will emphasize the dangers associated with this complication and stimulate physicians to diagnose transverse presentation either before or early in labor. Proper management of patients with this complication will make it possible to deliver vaginally more patients with greater safety. A decrease in the number of neglected patients will reduce the frequency of contraction ring and ruptures of the uterus. The indication for cesarean section will decrease as the early treatment of transverse presentation improves.

I wish to emphasize the fact that we have not had a maternal death in any patient with a transverse presentation since 1941. Durng the past six years our fetal mortality, associated with this complication, has been reduced 24.7 per cent.

The sulfonamides, antibiotics, and whole blood have all contributed to the reduction in our fetal and maternal mortality and morbidity.

THE EFFECTS OF ANEMIA ON LABOR*

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THE purpose of this study is to investigate anemia in labor and to attempt to establish a relationship between prolonged labor and reduced hemoglobin values, regardless of the etiology of the latter.

Unfortunately, a search of the literature revealed no physiological experimentation on muscular response as correlated with oxygen tensions. However, it seems reasonable to assume that any impaired oxygen-carrying capacity of the blood will reduce the efficiency of the uterine musculature, and thus prolong labor.

Yet none of the standard textbooks of obstetrics mention anemia as a cause of prolonged labor or dystocia.

In the literature of the past 30 years we were able to find only brief and infrequent references regarding anemia in labor.

Read[1] says, "I have rarely seen a good example of natural labor in a woman whose hemoglobin had been allowed to remain below 70% from thirty-three to thirty-four weeks onwards . . . not infrequently labor is long, exhausting and painful with a slow recovery during the puerperium." McCormick[2] listed anemia as a cause of primary inertia.

After studying 290 consecutive labors, we[3] reported in April, 1948, that anemia apparently prolonged labor.

Material

The cases for the present study are composed of the material above mentioned plus 729 staff deliveries, consecutive except for exclusions mentioned below. The cases were observed between July 1, 1948, and April 15, 1949, at the University Hospital in Augusta, Ga.

All cases included were spontaneous deliveries without oxytocics and were full-term pregnancies. For obvious reasons all cases of multiple pregnancy, breech delivery, cephalopelvic disproportion, transverse and abnormal presentation, festuses weighing over 10 pounds, forceps delivery and cesarean section were omitted.

The total incidence of forceps deliveries and cesarean sections was only 0.5 per cent for each during the collection of the series.

In the series there were 698 multiparas and 321 primigravidas. The multiparas and primigravidas were each divided into two groups: those having hemoglobin above 11 gm. per 100 c.c. of blood and those with values below this figure.

The hemoglobin determinations were made by the Sahli-Hellige type hemoglobinometer and doubtful or borderline cases were frequently rechecked with the Fisher electrocolorimeter. Hemoglobin determinations were made in all patients when they entered the hospital in labor.

The reason for choosing the dividing line of 11 gm. of hemoglobin per 100 c.c. of blood was that Labate,[4] in studying the dilution or hydremia of blood in

19 women at term and ten days post partum, concluded that the lowest hemoglobin which may be considered physiologic is 11.3 gm. per 100 c.c. However, Oberst and Plass[5] found the water concentration of whole blood to be significantly increased during gestation, but to fall to a normal level as parturition was approached and to drop below normal at the time of delivery. They stated, "The hemoglobin content of cells is increased during labor, when it is approximately 7 per cent higher than in non-pregnant women." Although these two investigators do not concur on what constitutes normal hemoglobin concentration at term, neither considers a hemoglobin below 11 gm. per 100 c.c. as physiological.

The size of the pelvis was determined in each primigravida by the Torpin-Thoms roentgenopelvimeter and this coupled with lateral films of the uterus in which the fetal head size was fairly accurately determined definitely ruled out any cases of prolonged labor due to cephalopelvic disproportion. Lateral films of the abdomen were made in approximately two-fifths of the multiparas and a few who did not progress properly had x-ray pelvic measurements taken in addition, as in the primigravidas.

Labor was considered as beginning when the pains became regular every 20 minutes. The termination of labor was considered as the end of the second stage.

All of the primigravidas and about two-fifths of the multiparas received amnesic and analgesic drugs. These consisted of intravenous scopolamine hydrobromide with pentobarbital sodium or Demerol. Three-fifths of the multiparas were delivered by students under the supervision of an obstetrical resident without the use of any of these drugs. However, in all cases of abnormal or prolonged labor, appropriate sedation and general supportive treatment were given.

In the group of primigravidas, there were 244 with hemoglobin above 11 gm. per 100 c.c. of blood and 77 with values below this. The average time of labor for those with hemoglobin above 11 gm. was 15 hours, 11 minutes, and for those with hemoglobin below 11 gm., 18 hours and 16 minutes. In other words, the average time of labor in the group of anemic patients was 20.3 per cent longer than in the nonanemic (Table I).

TABLE I.   PRIMIGRAVIDAS

	NUMBER OF CASES	AVERAGE TIME OF LABOR	LONGER LABOR
Hemoglobin of 11 Gm. or above	244	15 hr. 11 min.	
Hemoglobin of less that 11 Gm.	77	18 hr. 16 min.	20.3%

In the group of primigravidas, there were 67 cases of occiput posterior. Nineteen of these patients had hemoglobin values below 11 gm. and the average time of labor for these mothers was only 16 hours, 10 minutes; so we may exclude this as a factor in the above results.

There were 698 multiparas of whom 441 were classified as having adequate hemoglobin. The remaining 257 had hemoglobin below 11 gm. per 100 c.c.

The average time of labor for those with hemoglobin values above 11 gm. was found to be 10 hours and for those with hemoglobin below 11 gm., 12 hours, 17 minutes. Thus the average time of labor for the multiparas with the abnormally low blood findings was 22.9 per cent longer than for those considered normal (Table II).

TABLE II.   MULTIPARAS

	NUMBER OF CASES	AVERAGE TIME OF LABOR	LONGER LABOR
Hemoglobin of 11 Gm. or above	441	10 hr.	
Hemoglobin of less than 11 Gm.	257	12 hr. 17 min.	22.9%

The fetal presentation in 278 multiparas was definitely determined by x-ray. Forty-four of the fetuses were found in occiput posterior presentation. Thirty of the mothers had hemoglobin above 11 gm. and their average time of labor was 9 hours, 11 minutes. The average time of labor for the 14 mothers in the group with anemia was 17 hours, 45 minutes. This is much longer than the average for the entire series. However, one patient had a hemoglobin of only 9 Gm. and had dystocia for 72 hours before going into true labor and pushing the head into the midpelvis where the posterior position might have become a factor in prolonging labor. If we exclude this case, the average time in the remaining 13 cases is 12 hours, 19 minutes, which is almost exactly the average time for anemic multiparas. Therefore, we conclude that occiput posterior position had little to do with our final results.

This is in agreement with Calkins, Litzenberg, and Plass,[6] who could find no relationship between the presentation of the fetus and the length of labor.

Before analyzing the series for the incidence of prolonged labor and dystrophic dystocia it is necessary to define these terms. Prolonged labor is any labor with a duration of more than 24 hours. Dystrophic dystocia is defined as an abnormal labor in which the uterine contractions are irregular in frequency, duration, and intensity, with a high intercontraction tone.

Many causes have been ascribed to these conditions, chief of which is a disproportion between some part of the pelvis and the fetus. Other causes are mechanical obstruction by tumors, undue anxiety of the mother, hypopituitarism, pendulous abdomen, overstretching of the uterus by multiple pregnancy and polyhydramnios, toxemia of pregnancy, dehydration, and rigidity of the soft parts. With few exceptions we have been unable to find anemia listed, in the literature of the past 30 years or in the textbooks, as a cause of dystocia.

However, from a study of our cases it will be noted that the incidence of prolonged labor and this type of dystocia is considerably greater in anemic patients.

Of the 77 primigravidas with hemoglobin values below 11 gm., 17, or 22.1 per cent suffered prolonged labor and/or dystrophic dystocia. Of the 244 patients with hemoglobin above 11 gm. only 35, or 14.3 per cent, had prolonged labor and/or dystocia (Table III).

TABLE III. PRIMIGRAVIDAS

	TOTAL NUMBER OF CASES	CASES OF PRO- LONGED LABOR AND/OR DYSTOCIA	PER CENT OF TOTAL
Hemoglobin above 11 Gm.	244	35	14.3%
Hemoglobin below 11 Gm.	77	17	22.1%

Of the 257 multiparas with hemoglobin below 11 gm., 32, or 12.4 per cent, were found to have dystocia and/or prolonged labor. Only 30, or 6.8 per cent of the 441 patients with hemoglobin values above 11 gm. had prolonged labor and/or dystocia (Table IV).

TABLE IV. MULTIPARAS

	TOTAL NUMBER OF CASES	CASES OF PRO- LONGED LABOR AND/OR DYSTOCIA	PER CENT OF TOTAL
Hemoglobin above 11 Gm.	441	30	6.8%
Hemoglobin below 11 Gm.	257	32	12.4%

Comment

We are aware of the compensatory mechanisms which take place in the human body in many pathological states, including anemia. It would be too presumptive to assign any such simple cause as oxygen lack to the disturbed physiology of the uterus without actually measuring the oxygen supply per minute passing through an artery to this organ. Probably no single deficiency ever exists in the body alone. We feel that anemia indicates other deficiencies with their attendant biochemical and kinetic disorders.

Summary

In the literature of the past 30 years there are only brief, infrequent, and contradictory statements regarding anemia as an etiological factor of dystrophic dystocia and/or prolonged labor.

In the 1,019 patients studied there were 321 primigravidas and 698 multiparas. All patients with hemoglobin determinations below 11 gm. per 100 c.c. of blood were classed as anemic and those with hemoglobin above this figure were considered to have adequate hemoglobin levels.

Among the primigravidas there were 244 patients with hemoglobin determinations above 11 gm. and their average time of labor was 15 hours, 11 minutes. The 77 patients with hemoglobin below 11 gm. had an average length of labor of 18 hours, 16 minutes. This represents an average increase of 20.3 per cent.

In the group of multiparas there were 441 with hemoglobin determinations above 11 gm. and their average time of labor was 10 hours. The remaining 257 patients with reduced hemoglobin values had an average length of labor of 12 hours, 17 minutes, or an average increase of 22.9 per cent.

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UNIVERSITY HOSPITAL.

THE EVALUATION OF IRRADIATION THERAPY FOR NONMALIGNANT UTERINE BLEEDING AT THE UNIVERSITY OF VIRGINIA HOSPITAL*

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IT IS the purpose of this study to evaluate the results and complications of irradiation therapy for benign uterine or endometrial bleeding. There were 348 cases treated by intracavity irradiation or by roentgen-ray therapy in the University Hospital from 1925 to December, 1948, in which the initial pathological specimens were available. There was no pathological evidence of malignancy at the time of the original treatment in any of the reported cases.

TABLE I. AGE AT TIME OF TREATMENT

AGE IN YEARS	1925-1929	1930-1939	1940-1948	TOTAL
24 to 35	10	6	0	16
35 to 39	7	7	4	18
40 to 49	46	51	105	202
50 and over	19	27	66	112
Total	82	91	175	348

The cases are summarized in Table I. The ages of the patients ranged from 24 to 80 years at the time of the initial irradiation therapy. The average age for the entire group was 47.5 years. This is about the expected age of spontaneous menopause in this country.[1] No patients younger than 35 years of age have been treated since 1940. The majority of the patients, 314 of the entire series of 348, were 40 years of age or above. Three patients were above 65 years of age: one, 69 years, one, 72 years, and one, 80 years of age.

TABLE II. DIAGNOSIS AT TIME OF TREATMENT

	CASES	FOLLOWED	COMPLICATION MALIGNANT	COMPLICATION NON-MALIGNANT
Bleeding with fibromyomas	79	42	2	10
Bleeding without fibromyomas	269	136	6	16
Total	348	178	8	26

Table II shows the clinical condition for which irradiation treatment was instituted. The diagnosis of fibromyoma was usually a clinical diagnosis, and in all cases was associated with abnormal uterine bleeding. The remainder of the cases presented abnormal uterine bleeding without evidence of fibromyomas. Histologically, the endometrium showed the various phases of the menstrual cycle as well as atrophy and hyperplasia. In no case was there evidence of malignancy at the time of the initial therapy.

In Table III, the cases are grouped according to the amount of irradiation received. Two hundred fifty-nine patients, or 74.1 per cent of the series, received 1,500 to 3,000 mg. element hr. of irradiation. In this respect, it is interesting to

note that Schmitz and Towne[2] believe that a radium dosage of about 1,800 mg. hr. assures complete amenorrhea. During the past decade, a definite tendency to increasing amounts of irradiation is noted. This is probably the result of recurrent bleeding associated with the use of small dosages.

TABLE III.   AMOUNT OF IRRADIATION

MG. HR.	800 TO 1,200	1,201 TO 1,500	1,501 TO 2,000	2,001 TO 2,500	2,501 TO 3,000	X-RAY 3,200 ROENTGEN SKIN DOSAGE
1925-1929	39	10	18	12	3	0
1930-1939	19	13	39	18	2	0
1940-1948	0	6	16	126	25	2
Total	58	29	73	156	30	2

One hundred seventy-eight patients, or 51.2 per cent of the series, were followed from six months to twenty-one years, with the exception of two cases. One of these patients died four months after, and as a result of, pelvic irradiation. The other came to hysterectomy later, the exact interval being unkown.

TABLE IV.   FOLLOW-UP.   178 CASES FOLLOWED IN SERIES OF 348 CASES

	COMPLICATIONS		
INTERVAL	MALIGNANT	NONMALIGNANT	NO COMPLICATIONS
6 months to 2 years	0	6	23
2 years to 5 years	3	8	48
5 years to 10 years	1	3	34
10 years and over	4	7	39
Total*	8	24	144

*One case of pelvic tuberculosis followed less than six months. One case with subsequent hysterectomy, interval unknown.

It is noted in Table IV that one-half of the malignancies following pelvic irradiation occurred ten years or longer after initial therapy; conversely, more nonmalignant complications occurred during the first five years after treatment. Thus, it would seem that prolonged follow-up is necessary in evaluating the end results of pelvic irradiation.

TABLE V. MALIGNANT NEOPLASMS IN WOMEN PREVIOUSLY TREATED WITH PELVIC IRRADIATION

CASE	AGE (YEARS)	ORIGINAL DIAGNOSIS	IRRADIATION	INTERVAL (IN YEARS)	TUMOR TYPE
1	48	Atypical hyperplasia of endometrium	2,400 mg. hr.	4½	Adenocarcinoma of endometrium
2	63	Cervical or endometrial polyp	1,500 mg. hr.	11	Carcinoma of endometrium
3	53	Hyperplasia of endometrium	2,425 mg. hr.	3	Papillary adenocarcinoma of uterus, cervix and ovary. Origin undetermined
4	42	Hyperplasia of endometrium	2,000 mg. hr.	14	Adenocarcinoma of endometrium. Fibrosarcoma of uterus
5	55	Hyperplasia of endometrium	2,400 mg. hr.	13	Leiomyosarcoma of uterus
6	33	Clinical fibromyoma Secretory endometrium	1,200 mg. hr.	16	Sarcoma of uterus probably arising in endometrium
7	43	Proliferative endometrium	2,486 mg. hr.	5¾	Epidermoid carcinoma of cervix
8	55	Clinical fibromyoma Hyperplasia of endometrium	2,400 mg. hr.	4½	Papillary cystadenocarcinoma of ovary

Eight patients, or 2.3 per cent of the group of 348 patients, subsequently developed malignancy of the pelvic viscera. Of these eight patients, three developed adenocarcinoma of the endometrium. The interval between the initial irradiation therapy and the diagnosis of malignancy in these three cases were fourteen, four and one-half, and three years. A fourth patient developed papillary adenocarcinoma three years after treatment, which involved the cervix, uterus, and ovary with the origin pathologically undetermined. The original pathological diagnosis in three of the above four cases was hyperplasia of the endometrium. In the remaining case, the original diagnosis was polyp of endometrial or cervical origin. Corscaden, Fertig, and Gusberg,[3] and more recently Speert and Peightal,[4] have noted an apparently high incidence of endometrial hyperplasia in the uteri which subsequently develop carcinoma. The possible role of irradiation as a carcinogen in these cases was fully discussed by the latter group.

Of these eight patients, three eventually developed sarcoma. Two were of myometrial origin, and the third apparently originated in the endometrium. One of these patients, in addition to a fibrosarcoma of the myometrium, developed adenocarcinoma of the endometrium, and was previously included with those showing the latter pathological entity.

Of the two remaining patients in this group of eight, one developed carcinoma of the cervix five and three-fourths years after the original therapy, and the other developed adenocarcinoma of the ovary four and one-half years after having received intracavity radium, at the age of 55 years, for endometrial hyperplasia. Within the past three months, we have seen one other who developed adenocarcinoma of the endometrium, without bleeding, seventeen years after the initial irradiation. This patient is not included in this series due to lack of endometrial specimen for pathological examination at the time of irradiation therapy.

Twenty-six patients, or 6.4 per cent of the total of 348 patients, developed nonmalignant complications. Of this group there was recurrence of bleeding at intervals varying from ten months to ten years in ten patients in whom no further treatment other than curettage was instituted. The amount of irradiation in these ten cases varied from 800 to 2,400 mg. hr., and in no case was there additional irradiation therapy. Whenever possible, malignancy was ruled out by appropriate diagnostic procedure. However, in some instances further diagnostic evaluation was refused by the patient.

Eight of this group of 26 patients subsequently underwent hysterectomy for recurrence of bleeding. Fibromyomas of the uterus were associated with this bleeding in only 3 cases. Initial irradiation consisted of 800 to 1,500 mg. hr. in 3 of the cases, and of more than 2,400 mg. hr. in the remaining 5 cases.

Three of these 26 patients received additional irradiation therapy for recurrence of bleeding, at intervals of one and three-fourths years, three and one-sixth years, and two and one-half years. Initial irradiation therapy in these cases consisted of 1,200, 1,500, and 1,256 mg. hr. of radium, respectively. One of these patients subsequently developed pyometra following the second application of radium. Two others who did not receive additional irradiation therapy also developed pyometra or cervical stenosis. These three cases of pyometra or cervical stenosis responded to conservative therapy.

Of the three remaining patients in this group with nonmalignant complications, the first, a woman aged 46 years at the time of the initial therapy, came to laparotomy eleven years later for removal of a large ovarian cyst. The second who received initial irradiation for a supposed fibromyoma, had an exploratory operation six years later for enlargement of the tumor mass and was found to have a dermoid cyst of the ovary and no fibromyoma. The third died as the re-

TABLE VI. NONMALIGNANT COMPLICATIONS IN WOMEN PREVIOUSLY TREATED WITH PELVIC IRRADIATION

CASE	AGE	ORIGINAL DIAGNOSIS	IRRADIATION	INTERVAL (IN YEARS)	SUBSEQUENT COMPLICATIONS AND TREATMENT
1	53	Atrophy of endometrium	1,500 mg. hr.	10	Bleeding not fully investigated
2	30	Endometrial polyp	1,425 mg. hr.	10	Cyclic bleeding Not investigated
3	40	Hyperplasia of endometrium	2,000 mg. hr.	2⅛	Bleeding. D and C. No subsequent follow-up
4	44	Proliferative endometrium	2,100 mg. hr.	7	Bleeding. D and C.
5	33	Fibromyoma clinical Interval endometrium	1,200 mg. hr.	8	Cyclic bleeding to age 41 with spontaneous cessation
6	39	Endometrial hyperplasia	2,419 mg. hr.	1½	Bleeding. D and C.
7	40	Fibromyoma. Hyperplasia of endometrium	2,400 mg. hr.	2	Bleeding. Refused treatment
8	56	Fibromyoma. Hyperplasia of endometrium	2,400 mg. hr.	1	Bleeding. Not investigated
9	30	Hyperplasia of endometrium	800 mg. hr.	1¼	Metrorrhagia. D and C.
10	24	Secretory endometrium	800 mg. hr.	10	Bleeding not investigated
11	46	Secretory endometrium	2,427 mg. hr.	1½	Bleeding; pyometra Total hysterectomy
12	46	Fibromyomas. Hyperplasia of endometrium	2,636 mg. hr.	1½	Bleeding. Hysterectomy
13	48	Benign endometrium	1,500 mg. hr.	7	Hysterectomy elsewhere
14	51	Hyperplasia of endometrium	3,200 r	3	Bleeding. Hysterectomy
15	54	Fibromyomas. Hyperplasia of endometrium	3,000 mg. hr.	unknown	Bleeding. Hysterectomy elsewhere and died of peritonitis
16	32	Normal endometrium	1,000 mg. hr.	2	Bleeding after 12 months Hysterectomy
17	46	Fibromyoma. Hyperplasia	3,000 mg. hr.	1	Bleeding. Hysterectomy
18	29	Normal endometrium	800 mg. hr.	10	Menorrhage. Hysterectomy
19	36	Acute endometritis Fibromyoma clinical	1,200 mg. hr.	1¾	Bleeding. 3,200 r, four portals
20	50	No endometrium Fibromyoma	1,500 mg. hr.	3⅙	Bleeding. D and C. 2,400 mg. hr. radium
21	43	Secretory endometrium	1,256 mg. hr.	2½	Bleeding. 1,700 mg. hr. radium. Pyometra
22	34	Small fibroid. Hyperplasia of endometrium	800 mg. hr.	8	Bleeding; pyometra
23	51	Atrophy of endometrium	1,500 mg. hr.	15	Bleeding; cervical stenosis
24	46	Secretory endometrium	1,800 mg. hr.	11	Laparotomy. Large ovarian cyst
25	43	Interval endometrium Clinical fibromyoma	1,800 mg. hr.	6	Tumor enlargement Laparotomy. Dermoid cyst instead of fibroid found
26	40	Hyperplasia of endometrium	1,800 mg. hr.	⅛	Pelvic cellulitus. Acute exacerbation pelvic tuberculosis. Expired in four months

sult of therapy. This patient received intracavity radium for menorrhagia in an unrecognized pelvic tuberculosis. She was readmitted to the hospital six weeks after radium therapy with widespread pelvic dissemination of the tuberculous process, and died four months after original therapy. These last two cases illustrate that it is not always possible to exclude cases in which pelvic irradiation is contraindicated.

Summary

1. Three hundred forty-eight patients receiving pelvic irradiation for benign uterine bleeding have been presented.

2. With the exception of two cases, 178, or 51.2 per cent of these patients have been followed from six months to twenty-one years after the initial treatment.

3 There were 26 nonmalignant and 8 malignant complications which subsequently developed.

4. One patient died as the result of intracavity irradiation in an unrecognized pelvic tuberculosis.

Conclusions

1. It would seem that surgery with preservation of ovarian function is preferable to pelvic irradiation in those women 40 years of age or younger. In our clinic, only four women in this age group have received pelvic irradiation since 1940.

2. Intracavity irradiation is such a simple technical procedure that one is prone to fail to appreciate the possible complications that may subsequently develop. Thirty-four, or 9.8 per cent of the entire series, developed some complications after the original pelvic irradiation.

3. We believe that prolonged subsequent follow-up is imperative in those women who have received pelvic irradiation for benign uterine bleeding. One-half of the malignancies have occurred ten years or longer after initial therapy.

4. In spite of careful selection of patients, it is not always possible to exclude cases in which pelvic-irradiation is contraindicated.

5. At the present time we reserve pelvic irradiation for those patients with benign endometrial bleeding requiring treatment, who have some contraindication to major surgery.

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    921 RUGBY ROAD

VASA PREVIA*

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AMONG the obstetrical complications producing vaginal bleeding in the late prenatal period or after the onset of labor, vasa previa is seldom mentioned in the obstetrical literature. This condition is rarely diagnosed before rupture produces hemorrhage, thus creating a severe hazard to the life of the baby, most often with a fatal outcome.

Vasa previa has been defined as "a condition in which the blood vessels of the umbilical cord where they enter the placenta present in front of the fetal head in labor."[1] As pointed out by Rucker and Tureman,[2] in their very comprehensive review of this subject in 1945, this definition is open to several objections. The patient need not be in active labor, the fetus need not present by the head, and the umbilical vessel need not be near the placenta. An aberrant vessel may rupture although the umbilical cord may have a normal or central implantation. Likewise, vessels branching between one or more lobes of a multipartite placenta or a placenta succenturiata may constitute a vasa previa if they cross the internal cervical os and are subject to rupture, either spontaneously or artificially. A velamentous insertion of the cord is usually present and many specimens of this anomaly have been encountered, often with the opening of the membranes near or between branches of the umbilical vessels which remain unruptured and therefore these cases are usually unreported in the literature.

In the following case spontaneous rupture of a vasa previa occurred prior to the onset of labor in a twin pregnancy, with immediate death in utero of the first twin, and the survival of the second twin following spontaneous delivery. The diagnosis of vasa previa was not made until after delivery was completed, although it was suspected due to the clinical course of the case associated with a known multiple pregnancy. Rupture of the velamentous vessel also occurred spontaneously in this case without rupture of the amniotic sac.

Mrs. F. P. W., a white multipara, aged 31 years, was admitted to the Virginia Baptist Hospital on June 13, 1947, for induction of labor at term. Her pregnancy has been essentially normal until April, 1947, at which time she was hospitalized for threatened premature labor at the seventh month. Following bed rest, sedation, and corpus luteum therapy, all contractions ceased. X-ray of the abdomen at that time confirmed the diagnosis of a twin pregnancy.

Physical examination revealed a tall, slender, poor nourished woman, whose abdomen was obviously larger than average for a full-term pregnancy. Two distinct fetal outlines could be palpated and two normal fetal heart tones were audible. The blood pressure was 118/78. There was no edema. The urine showed a faint trace of albumin and an occasional epithelial cell, the chemical examination being normal. Wassermann test was negative; hemoglobin 82 per cent; Blood type, 2; Rh factor, positive.

The past obstetrical history was significant only in the fact that her first pregnancy was terminated at full term by breech delivery, after a labor of six hours.

During the night of admission, the patient was awakened at 2:00 A.M. by a sudden and rather profuse painless vaginal hemorrhage. Immediate examination revealed the absence of the fatal heart tone on the left, while the fetal heart tone of the other fetus continued audible and normal. The maternal pulse rate was 64 and the blood pressure 120/78. Abdominal examination revealed no tenderness or rigidity. Bleeding ceased shortly after the

initial hemorrhage, and after 45 minutes mild uterine contractions began. Vaginal examination showed the cervix to be well effaced, quite soft, and dilated about 3 cm. There were neither placental tissue nor pulsating vessels palpable, and the amniotic sac was intact.
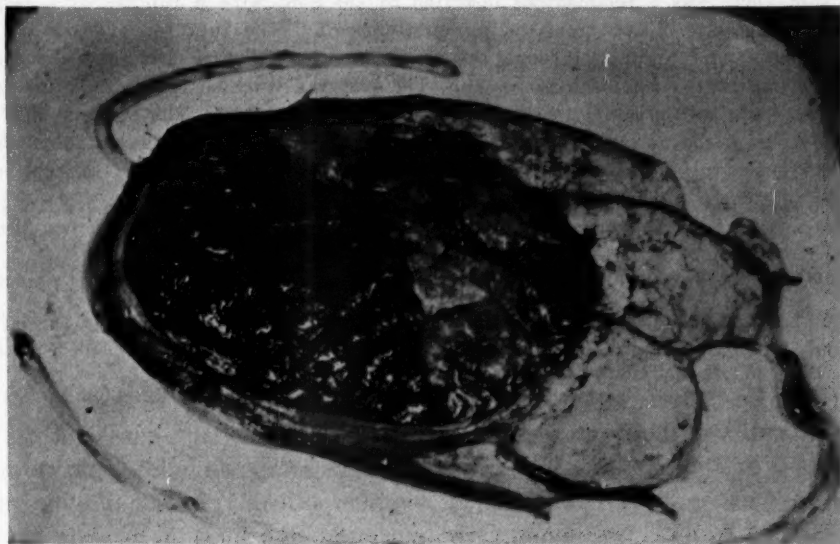
Fig. 1.—Maternal surface of the placenta, showing the pale, ischemic color of placenta on the side of the ruptured velamentous vessel, and the dark, normal appearance of the opposite half of the placenta.

Fig. 2.—The fetal surface of the placenta, showing the normal central insertion of the umbilical cord on one side, and the branching velamentous cord on the opposite side. The thrombosed ends of the large ruptured vessel are clearly seen, with two unruptured velamentous vessels in the membranes.

In view of these findings complicating a twin pregnancy, it was felt that a ruptured vasa previa most likely existed, although such a diagnosis could not be confirmed at this time. The membranes were ruptured artificially to stimulate labor and uterine contractions progressed rapidly. The first twin was delivered by forceps after approximately four hours

of labor and was stillborn. The second twin was delivered spontaneously fifteen minutes later, in excellent condition. The third stage of labor was normal and complete in eight minutes.

The placenta was of the large single variety with two amnions and a single chorion. On one side, there was a velamentous insertion of the cord with a rupture of a large vasa previa approximately 12 cm. from the placental margin. The ruptured ends of the vessels were thrombosed and coursing through the membranes on either side at some distance were two smaller unruptured velamentous vessels. The placenta revealed one-half of the maternal surface quite pale and ischemic on the side of the ruptured vessel. The opposite half of the placenta presented the normal, blue-purple color, and a normal central insertion of the cord.

Spontaneous rupture of the large vasa previa prior to labor resulted in almost complete loss of circulation to the first twin, with immediate death in utero.

The mother made an uneventful recovery and she and the living twin was discharged from the Hospital on the eighth postpartum day in good condition.

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511 ALLIED ARTS BUILDING.

Original Communications

OBSERVATIONS ON THE FETAL ASPECTS OF PLACENTAL CIRCULATION*†

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DURING recent years considerable speculation but little factual information has been forthcoming regarding the nature of blood flow within the human uterus throughout gestation. In the interim, hypotheses and theories have been propounded to explain the changes in placental steroid concentrations during the course of normal and abnormal pregnancy.[1, 2, 3] These changes which precede normal labor, premature labor, and pregnancy toxemia are assumed to be due to alterations in placental morphology, as affected by abnormal uterine blood flow. A correlation has been proposed between the steroid activity of the placenta and these modifications in its morphology.

The maternal portion of the placental site also undergoes morphological alteration during the course of pregnancy. The decidua appears to be in a continuous state of growth and regression,[4] and this process is supposedly increased as term approaches. The decidua, as the supporting stroma of the placental site, may adversely affect the spiral arterioles and placental sinusoids, should it degenerate. Disintegration of this tissue would allow for sudden collapse of these vessels with subsequent thrombosis or hemorrhage. If thrombosis occurs, a placental area supplied by compromised circulation will become infarcted. In the absence of thrombosis, hemorrhage would ensue followed by varying amounts of premature separation.

The recent studies of Reynolds on the pregnant uterus of the rabbit have demonstrated rather marked changes in the rate of blood flow during the different stages of pregnancy. Further, these studies revealed that marked alterations in shape of the growing uterus occurred during pregnancy in order to avoid catastrophic decreases in placental blood flow.[5, 6] From such evidence, the inference can be drawn that alterations of uterine blood flow produce uteroplacental ischemia resulting in morphologic changes at the placental site. These changes may be the underlying etiological factors of major pregnancy complications.

Until recently the opinion has prevailed that placental function could be explained simply on the basis of the fetal trophoblast serving as a semipermeable membrane. It can now be accepted that the placenta is a complicated organ having functions of a respiratory, renal, and metabolic nature. There is also reason to believe that active secretion across the trophoblast barrier occurs, which may involve an extensive enzyme system. The studies of Flexner and his co-workers[7, 8] using heavy water and an isotope of sodium have indicated the rapidity of water and electrolyte exchange. In spite of the marked decrease in the albumin and globulin ratio of the fetal blood when compared to maternal blood, the osmotic activity of the former does not allow the fetus to be depleted of fluid.[9]

There is evidence that the pressure within the umbilical vein contributes to the adequate filling of the fetal heart. However, the relatively few observations and the marked differences in the venous pressure values obtained from the umbilical vein are an indication of how little is known regarding the nature of this aspect of fetal circulation.[10] It is stated that the ratio between the blood volume of the fetus and of the placenta increases as pregnancy advances. This would indicate that rapid blood flow is necessary particularly during the latter part of pregnancy if the relatively large amount of blood contained within the fetus is to be adequately oxygenated. Similarly, the estimated minute blood flow within the placenta when correlated with the total fetal blood volume would suggest increased velocity of fetal placental blood flow.[9] Hence the rate of blood flow and the metabolic exchange necessary to meet the increasing needs of the fetus, as it develops during intrauterine life, demands that the placenta fulfill certain morphological criteria. For it to perform these functions, certain assumptions arise which are at variance with present concepts of placental architecture. These discrepancies between certain physiologic observations and present morphologic concepts suggested that the latter should first be restudied and reappraised.

The recent studies of early human ova have accurately recorded the morphology of the conceptus during the period of implantation.[11-14] During the formation of definitive chorionic villi, and prior to the time that fetal circulation is established, the ovum is sustained by what Ramsey prefers to call "nutrition by local pabulum."[15] This is derived from extracellular fluid, local hemorrhage, and disintegration of tissue cells surrounding the implantation site. This period ends approximately at the third week following implantation. By this time angiogenesis within the placental villi is sufficient to allow for fetal circulation to develop.[16] It is assumed that the fetal heart is now beating and a fetal placental blood flow is established.

The placenta now becomes a more complex organ. Its structure is limited by a decidual trophoblastic plate on the maternal side and a chorionic plate on its fetal aspect. Spreading over the latter and intimately adherent to it are the branching vessels arising from the umbilical arteries and veins. These vessels in turn branch to supply the main stem villi. There is a further division of vessels subsequent to the development of the secondary or terminal villi. Most villi lie

free within the intervillous space while some remain adherent to decidual connective tissue and have been termed "anchoring villi." Groups of these various villi constitute the formation of a cotyledon which is the functioning unit of the placenta.

The fetal placental circulation is confined to the vascular channels within the substance of the villous stroma. The maternal placental circulation is intimately related to it, but no known communications between the two systems are thought to exist. Maternal blood derived from the spiral arteries circulates within the intervillous space, bathes the trophoblastic syncytium across which metabolic exchange is presumed to occur, and, as venous blood, returns to the uterine veins. Blood circulating within the fetus passes to the placenta through the umbilical arteries, enters the villous system and is eventually returned volume for volume metabolically re-enforced by way of the umbilical vein.

The intricacies of the vascular patterns of the uteroplacental circulation in the maturing placenta have been emphasized in previous morphologic studies. Bumm[17] and Klein[18] working independently arrived at identical conclusions with respect to the vascular channels of the uteroplacental circulation of recently born placentas. The uteroplacental arteries were identified by their tortuosity and diminished blood content. It was their opinion that, as a rule, the spiral uteroplacental arteries were confined to the borders of the placental cotyledons, and particularly in the placental septae. The maternal arterial blood entered each cotyledonary unit at these sites, bathed the treelike branching villous system, and drained out through the central basal decidual portion as venous blood. The study emphasized the independent circuit and closed features of the fetal and maternal blood streams.

This work was the basis for the accepted concept of intervillous circulation until as recently as 1936, when Rudolph Spanner[19] sought to establish a new concept of maternal and fetal circulation within the placenta. He contended that an adequate explanation of the placental circulation involved proper consideration of changes relative to the in vivo activity of the uterus. The changes in the tonicity of the uterus transmitted to the placenta as well as the so-called villous impulse originating in the fetal circulation were mechanical factors contributing to the maternal blood flow within the intervillous space.

Spanner indicated that the criteria used by Bumm and Klein for identifying the arterial channels on the maternal side, namely, torsion and blood content, were not valid. In addition, he stated that in his opinion examination of their published illustrations failed to reveal differences between alleged arteries and veins, or the relationship of such arteries to their related septae. On the basis of injection-corrosion studies of intact uteroplacental sites, Spanner offered a revised concept of maternal flow. According to his work, spiraled uteroplacental arteries passed through the myometrium without establishing anastomosis, and ended in a definitive whirl tuft. The whirl tuft was composed of a series of convolutions each having a comparatively wide circumference which branched and terminated in narrow stem end pieces, which in turn opened into the intervillous space. The entrance of these end pieces into the intervillous space was

not restricted to the septae but involved the entire basal portion of the placenta. Spanner denied the existence of venous communications between uterine veins and centrally located cotyledons. He maintained that arterial blood entered at the base of the cotyledon, filled the intervillous space progressively within the confines of the septae, and, upon reaching the subchorionic area, flowed as venous blood toward the marginal zone. The return of venous blood to the uterine veins was accomplished through the marginal sinus and direct communications between the marginal zone and the myometrial veins. This was described as a unidirectional flow through the intervillous space and the over-all plan was a completely new idea.

With respect to the fetal aspects, Spanner proposed what has been termed the "chandelier" concept of villus arrangement. In arriving at the details of this scheme, he studied mostly born placentas in conjunction with some of the uteroplacental preparations. In his opinion, the fetal arteries and the fetal veins both have the same distribution within the stroma of the villi. With the exception of those branches which originate from the main divisions of the umbilical arteries and which are restricted to the surface of the placenta, he described the vessels within the substance of the placenta as being vertical to the fetal as well as maternal surfaces of the organ. Because of this parallel arrangement, Spanner questioned the previous concept of a widespread treelike distribution of the secondary villi and their vessels as they are derived from the primary stems. From his material, he described the larger vessels within the primary villi as running parallel toward the decidual surface and then reversing themselves to give a chandelier-like effect as they return in a vertical direction toward the chorionic plate. With this arrangement, the basal half of the placenta contained the greater number of vessels in contrast to the area beneath the chorionic plate. Although the arteries and veins pursued a similar course, they appeared macroscopically different. According to Spanner, the middle-sized and larger veins contained valvelike sphincters giving a configuration like a string of pearls to the external surface of the vein.

The studies of Spanner were chiefly concerned with maternal uteroplacental circulation. In his description of the morphology of the fetal aspect of blood flow, the observations were restricted principally to the large stem vessels. These included a beadlike configuration of middle and large-sized veins and the presence of an arrangement about the main stem vessels, not unlike the vasa vasorum. In the section devoted to a description of the shape of the intervillous space, it is suggested that, in villi other than primary, there is a long, wide capillary loop which connects with an artery and vein situated at the base of the villus. From the point of view of function, the capillary bed within the secondary villi would appear to be all important for it is these villi which continue to develop throughout pregnancy and play an increasingly important role in uteroplacental metabolic exchange. This suggests that a detailed study could be made profitably of the capillary bed of the placenta.

In the attempt to study the blood flow in the human uterus during pregnancy, initially the vascular patterns of freshly born placentas as well as a num-

ber of pregnant uteri removed by hysterectomy for therapeutic reasons were examined. These latter specimens, subjected to injection technique, furnish material for the examination of the intact uteroplacental site, but as yet these have not been studied in any detail. This communication is concerned only with recording some preliminary observations on the fetal aspects of the vascular pattern of the placenta.

Material and Methods

Normally born term placentas were used in this part of the investigation. The clinical histories of patients were reviewed and only placentas from normal pregnancies and deliveries were used. Immediately following expulsion each placenta was perfused with 500 c.c. of normal saline at approximately 38° C. through a cannulated umbilical artery. This accomplished the dual purpose of washing out the residual blood and also of maintaining the fetal vessels in a relaxed state. Vessel spasm may make cannulating the umbilical artery a difficult procedure. The placentas were injected with India ink, 12 per cent vinyl acetate, or liquid latex. India ink specimens were cleared by a modified Spalteholtz method described below according to Wislocki.[20] Arterial or simultaneous arterial and venous injections were completed. The arterial injections were performed at 120 mm. Hg while the venous injections were completed at 50 to 60 mm. Hg. In addition, injection of a more concentrated solution of plastic (28 per cent) combined with Fuller's earth was carried out at a pressure of 200 to 250 mm. Hg. This concentration was found to fill successfully the larger caliber vessels while it failed to enter the smaller channels. The smaller vessels were injected with 12 per cent vinyl plastic without filler at physiologic pressures after having been perfused with saline and followed by acetone.

Following injection, the India ink-treated organs were placed in 10 per cent formalin for a minimum of 48 hours. They were then cut in 1.0 cm. parallel slices which were dehydrated through absolute alcohol and cleared with benzene and oil of wintergreen. The plastic preparations were allowed to polymerize under cold running tap water for 2 hours and then were immersed in commercial concentrated hydrochloric acid for 24 to 48 hours. Following corrosion, the casts of the fetal vessels were washed with jets of tap water. The liquid latex preparations were immediately immersed in commerical hydrochloric acid for 48 hours and then recovered and washed. The cleared India ink preparations were cut by hand into thin sections which were examined under the dissecting microscope. With the aid of a pair of jeweller's forceps, portions of the fetal vascular tree were teased apart to allow for inspection and study.

Results

The plastic preparations are best suited for study of the arrangement of the basic vascular architecture. These readily reveal the complexity of the blood vessel distribution. For descriptive purposes it is convenient to discuss (a) the vessels of the allantochorionic surface, (b) the vessels which penetrate the substance of the placenta, i.e., the subchorionic vessels, and (c) the terminal branches of the blood channels, including the arrangement of the capillary vessels in the terminal villi. These divisions are arbitrary and it must be remembered that each so-called segment is a portion of a single unit.

The Allantochorionic Vessels.—

These major branches of the umbilical vessels are the main channels for distribution of fetal blood to and from the major parts of the placenta. The arteries are accompanied by veins, and in plastic preparations these are readily distinguishable from one another by differences in their relative diameters

(Fig. 1). The veins are approximately twice the diameter of the arteries. The umbilical arteries give rise to what we would term primary allantochorionic vessels. These in turn divide to form secondary branches and, from the latter, tertiary main stem channels originate. The primary and secondary branches are relatively few in number and considerably larger and longer than the tertiary branches which penetrate the individual lobules or cotyleodons. It is the
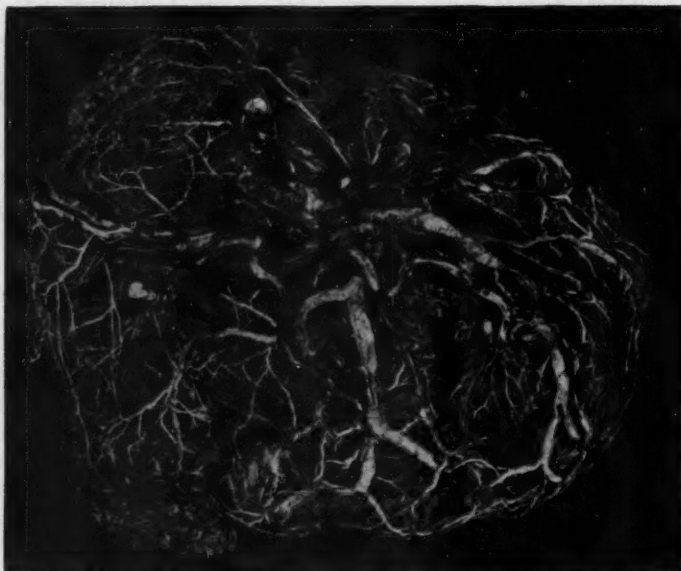
Fig. 1.—Allantochorionic artery and vein distribution.
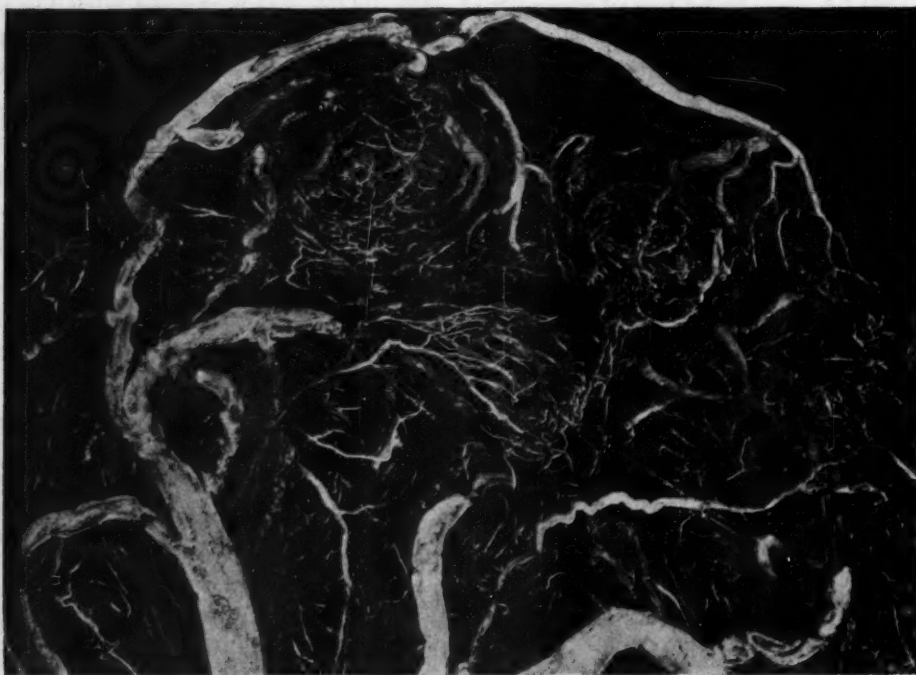
Fig. 2.—A dual arterial supply of a marginal cotyledon.

tertiary branches that exhibit a greater degree of arborization in which short small branches supply an individual lobule. Allowing for an accepted shrinkage of 20 per cent with vinyl acetate, the average diameters of primary, secondary, and tertiary main stem arterial vessels were 3.0 mm., 2.0 mm., and 0.7 mm., respectively; while on the venous side the respective diameters were 5.0 mm., 3.0 mm., and 1.2 mm. An unusual feature occurring in a majority of the marginal cotyledons is a dual arterial supply in contrast to the single vessel which supplies the central cotyledons (Fig. 2).

Fig. 3.—An arterial cast showing subchorionic distribution of vessels of the caliber of main stem channels.
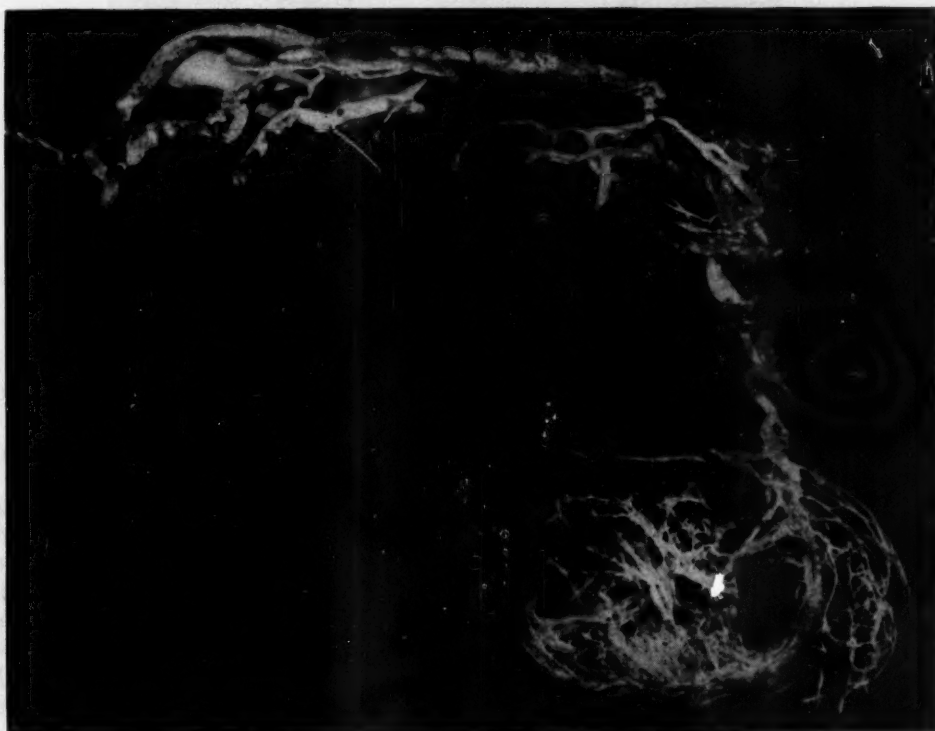
Fig. 4.—Origin of a spiraled arterial vessel with terminal cotyledons.

Subchorionic Vessels.—

Observations on the vascular arrangements of the vessels penetrating the substance of the placenta were accomplished by utilizing the corroded vinyl acetate casts and undiluted India ink-injected material.

Fig. 5.—Spiraled arterial structure in various phases of coiling.

The plastic preparations provided three dimensional models and general orientation. The injected India ink material, when cleared, allowed minute examination of the structure of the villous system, and the finer ramifications of arterioles, venules, and the capillary network. Fig. 3 is a close-up photograph of a portion of an arterial cast made with the more concentrated solution. It reveals that vessels of the caliber of main stem and anchoring villi branches are distributed throughout the substance of the placenta between chorionic and decidual plates. There is a concentration of such channels near the basal surface but such vessels are also seen in numbers beneath the chorion. When the 12 per cent plastic was introduced into the arterial system under physiologic pressures, a similar distribution of primary and anchoring villi vessels was noted. However, in addition, primary villus stem arteries exhibit a spiraled nature.[21] The spiraled villus vessel arises at a right angle to the chorionic plate from the large chorioallantoic vessels (Fig. 4). It forms a helix of slowly diminishing diameter as it passes toward the decidual plate. The number of

coils observed varied between two and five. Some of these appear to be uncoiling and others are paid out (Fig. 5). The spiraled fetal subchorionic arteries, without exception, pass to the region adjacent to the decidual surface.

The difference in diameters between arteries and veins observed in the chorioallantoic vessels in no longer apparent beneath the chorion. Main stem arteries and veins appear to have the same caliber, with the exception of the specialized spiraled structure with its helical arrangement of diminishing diameter (Fig. 4). There is a rather marked decrease in the relative diameters between the terminal spiraled segments and the delicate vascular components of the cotyledonary tufts.

Fig. 6.—Concentrated plastic corrosion cast of large veins. No valves seen.

Because Spanner reported the macroscopic beadlike appearance of the middle- and large-sized fetal veins produced by intrinsic valvelike structures, a series of placentas were injected through the umbilical veins with 12 and 28 per cent plastic with and without filler. No gross alterations could be identified either of the medium-sized veins of the primary villus, or of the large-sized chorioallantoic veins (Fig. 6). India ink-injected placentas failed to reveal any constrictions or distortions suggestive of intrinsic or extrinsic muscular sphincters.

From initial observations, it appears that the chorionic villi are supplied by three types of linear vessels: (1) Relatively long vessels in the primary and

anchoring stem villi, some of the former being spiraled, which supply the region of the basal plate; the subchorionic zone is supplied by (2) relatively short channels; while the remainder, involving approximately the mid-zone is supplied by (3) vessels of intermediary length.

Terminal Branches and Capillaries.—

The striking feature of the arrangements of the terminal vascular branches and capillary network of the mature placenta is the widespread distribution of vessels of this caliber involving the entire substance. Vascular channels of capillary dimensions are situated at all levels between the decidual and chorionic plates. Fig. 7 is a decidual view of a corroded arterial cast, which demonstrates the extensive terminal components of the vascular bed of the mature placenta. There is a definite concentration of vessels in the region of the basal plate which becomes less dense beneath the chorion. Under a binocular microscope, examination of a cast made of simultaneously injected arteries and veins indicates that, in well-injected regions, the arterial supply and venous drainage almost meet. In no case was the distance between an artery and the adjacent beginning of a vein more than about 1 mm. and usually it was less. Inasmuch as it was our observation that 12 per cent vinyl acetate without filler would inject vessels of arteriole-venule dimensions, these findings provided evidence of the relative shortness of the capillary bed.
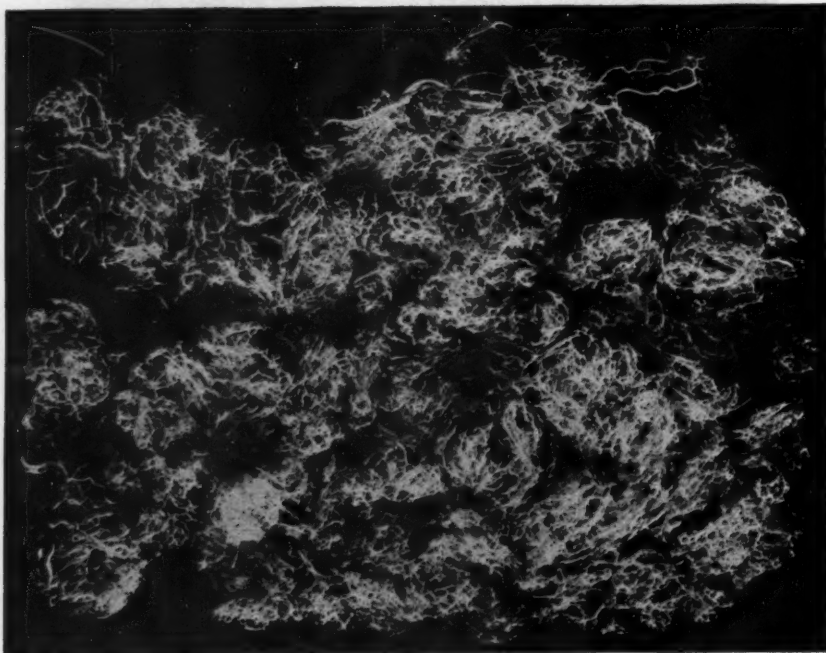
Fig. 7.—Decidual surface view of placental cast, demonstrating extensive terminal arterial bed.

With these observations as a background, India ink-injected cleared material is being studied in order to gain an insight into the nature of the capillary bed. The details of the capillary network and the structure of the villous system will be further investigated by serial section reconstruction. However, as a result of analysis by dissections of cleared preparations, certain findings appear significant. There is a difference in the type of capillary network which one sees near the fetal surface as compared to the maternal side of the placenta. Furthermore, the terminal villi near the chorionic third differ from those in

the region of the basal plate. The former are thin, elongated, and appear to dangle free in the subchorionic zone of the intervillous space. The capillary arrangement of such villi involves sinusoidal connections between a slender
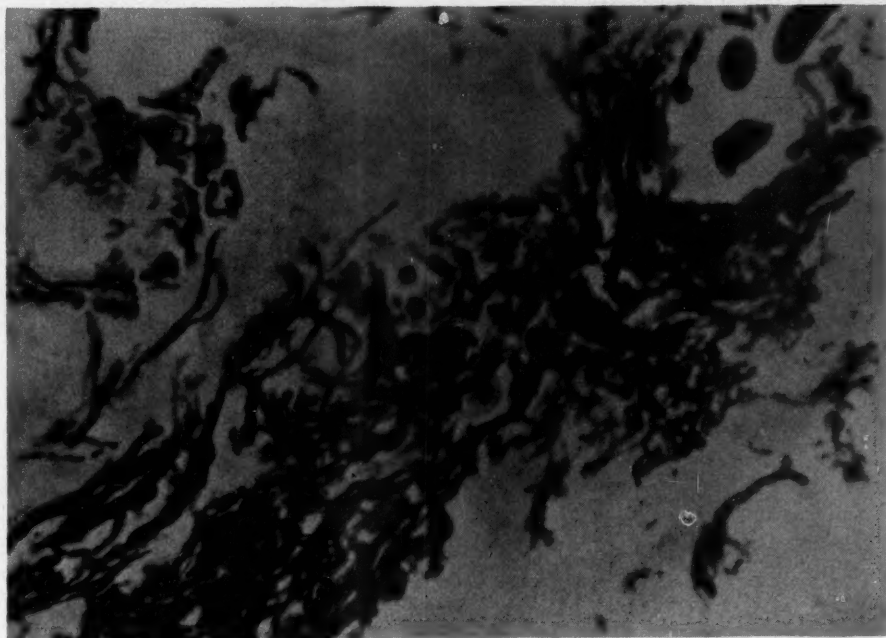
Fig. 8A.—Photomicrograph of the capillary arrangement in the subchorionic region.

Fig. 8B.—Anatomic drawing of capillary arrangement in subchorionic region.

arterial component and more prominent venous channels. Such channels are usually found at the periphery of the villi. The capillaries of terminal villi average 5 to 10 in number and are characterized by their relative shortness (Fig. 8, A and B).

By contrast the terminal villi of the basal third of the placenta, which are derived from the longer main stem elements, are much more numerous, relatively blunt, and considerably shorter. Because of their great numbers, they are densely packed together with the result that, in cleared preparations, the inter-villous space is not easily seen. These villi exhibit the greatest degree of arborization of the entire villous system yielding short end stems. The capillary bed appears most extensive in this region and is composed of short, wide channels, which occupy almost all of the villous stroma. Extensive branching is similarly observed in the capillary buds and forms small plexiform units compared to the sinusoidal arrangement of the fetal zone. (Fig. 9, *A* and *B*). The intermediate zone between the fetal and maternal regions shows a gradual transition between the two types of capillary arrangements with a preponderance of the basal components.

From these preliminary observations, the capillary units regardless of location appear to be short. These findings do not substantiate Spanner's speculation of a relatively long capillary bed connecting with venous channels at the base of the villus.

Comment

The intimate vascular relationship of the maternal and fetal circulations within the placenta complicates investigation of its morphology. There is uniform agreement that within the myometrium the spiraled arcuate arteries under the influence of pregnancy undergo hypertrophy and growth. Those in the region of the uteroplacental site are known to supply the intervillous space though there is disagreement as to the exact entrance of the arterial supply with relation to placental septae and the basal plate. Within the confines of the intervillous space, maternal flow has been described in one manner by Hinselmann[22] and in still another by Spanner.[19]

Several of the observations in this study are at variance with the chandelier concept of fetal vascular channel distribution as proposed by Spanner. Vessels of the caliber within main stem villi have been observed originating and being distributed at all levels between the decidual and chorionic plates. Such vessels rapidly diminish in caliber and assume an order of magnitude of arterioles, arteriolar capillaries or basic capillary bed, which characterizes the bulk of the fetal placental vasculature. Only those vessels of main stem or anchoring villi which supplied the zone adjacent to the decidual plate were observed to reverse their course and give a suggestive chandelier-like configuration. No evidence was obtained to support the conception of a long capillary villous loop, running the length of the villus, connecting the artery and vein, situated at the base of the villus. Instead, the findings indicate a short, though extensive capillary network. This short length of the capillary bed conceivably is the morphologic feature which is essential to adequate venous return to the fetus. Thus while arterial blood is distributed to an extensive capillary network, the shortness of the bed provides for a minimal dissipation of energy in order to maintain constantly a pressure capable of assuring venous return. Corroborating the findings of Bacsich and Smout,[23] this study failed to find any bead-like structures related to the fetal veins which according to Spanner were due to valvelike structures within the veins, and which he suggested fulfilled two functions. Contractions of the sphincters with resultant stasis in the capillaries of the villi favored an increase in the metabolic exchange between maternal and fetal blood. Furthermore, under these conditions, Spanner stated, a temporary increase in the blood volume of the villi developed, which exerted an influence on the maternal blood mass flowing in contact with the villi.

For the first time, attention has been drawn to the differences between the architecture of the vascular bed of the villi situated beneath the chorionic plate

Fig. 9A.—Photomicrograph of vascular injection of capillary arrangement near decidual plate.

Fig. 9B.—Drawing of capillary arrangement adjacent to decidual surface.

and those near the basal side. In the subchorionic area they are long and sinusoidal in design while in the decidual zone, the arterioles and venules are much shorter and plexiform in arrangement. Thus, in both instances, the capillaries are short, and the differences observed have been in the length of the arteriole and venule component. These variations of the fetal vascular bed in different zones of the placenta permit speculations as to function.

Oxygen appears as the sole constituent which must be continuously supplied to the growing fetus. Other metabolic activity within the placenta necessary for proper fetal growth may be completed with less urgency. Hence, it is conjectured whether the marked concentration of villi with their plexiform vascular arrangement adjacent to the basal plate may be a respiratory zone. The maternal blood entering the intervillous zone would encounter the dense plexiform vascular bed within the terminal villi. This would be conducive to immediate oxygen, electrolyte, and carbon dioxide exchange. In contrast to this, the subchorionic region with its sinusoidal vasculature pattern is better adapted for such energy consuming processes as filtration and secretion. It is thus postulated that this zone may be for intermediary metabolism of carbohydrates, proteins, and fats.

The existence of main stem fetal vessels in the placenta which are spiraled is noteworthy in view of present thinking with regard to this morphologic feature. Spiraling has been observed in the vasculature of ovary, myometrium, and uterus. It has been suggested that it is a manifestation of rapid growth under the trophic stimulus of steroid hormones.[24] The human placenta is well known as a site of abundant formation of steroid hormones throughout the course of pregnancy. By analogy, the occurrence of spiraling in fetal stroma may be attributable to a similar response. Functionally, this spiral pattern is no doubt important in maintaining a constant gradient of pressure to the fetal capillary to make possible an adequate fetal to maternal exchange through a constantly effective hydrostatic pressure.

Summary

1. The fetal vascular ramifications of the human placenta have been studied with a variety of injection techniques. Vinyl acetate injected placentas have been corroded. India ink-injected material has been cleared with a modified Spalteholtz procedure.

2. The intimate nature of the relationships of maternal and fetal vascular channels within the placenta has been a major source of difficulty in study of the uteroplacental circulation.

3. The fetal capillary network though extensive has been found to be short in linear magnitude. This morphologic feature may be basic in the mechanism of adequate venous return. No beadlike medium or large-sized veins have been identified.

4. Spiraled fetal main stem vessels of the placenta, by analogy, may reflect a response of trophic stimulation of steroid hormones, previously suggested for the ovary, myometrium, and endometrium. It allows for a gradient of pressure to the capillary bed.

5. The capillary network of the subchorionic zone is sinusoidal in nature. The area adjacent to the decidual plate, in contrast, has a plexiform arrangement. This morphologic discrepancy suggests diverse functional activity in the various zones of the placenta.

We would like to acknowledge with thanks the helpful suggestions and advice of Drs. George B. Wislocki, Samuel R. M. Reynolds, and Arthur T. Hertig during different phases of this investigation. We are indebted to Mr. Chester Reather for much of the photographic material. The anatomical drawings were kindly done by Miss E. Piotti.

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221 LONGWOOD AVENUE

Discussion

DR. GEORGE W. BARTELMEZ, Chicago, Ill.—Only those of us who have injected animals under the most favorable conditions can fully appreciate the difficulties of making as perfect injections as Dr. Reid has shown here and these from an organ which has gone through the ordeal of labor. Corrosion methods are absolutely essential for work of this kind. It is difficult to follow the circulation in the endometrium but when you come to the placenta you are absolutely lost unless you can dissect out individual vessels. Latex injections make that possible. I feel that Dr. Reid's injections have been very much better on the fetal side than anything Spanner had. The distinction between the two areas in the placenta appeals to me very much, particularly in view of the observations that Flexner, Gellhorn and others have recently made. They demonstrated that every 2.9 hours the amniotic fluid in the human uterus is completely changed. Where does all of it go to? Perhaps it escapes by way of the placenta, diffusing through amnion and chorion plate. I was reminded of an experience with a specimen brought to me by Dr. Cornell about 35 years ago. He submitted what proved to be a normal 5 months' pregnancy in a myomatous uterus. When the intact uterus with the vessels clamped was brought out from the operating room, I palpated the placental area and cut through the myometrium. Large vessels were missed so there was practically no bleeding. The fluid that gushed from the placenta was not blood. The intervillous space was filled with a pale yellowish fluid. If the intervillous space were gradually being dilated by amniotic fluid as well as maternal blood it would explain the situation very well. It is difficult for me to see how the fluid in the intervillous space could stay there longer than between two myometrial (Braxton Hicks) contractions. When a normal pregnant uterus contracts there is nothing that can give way except the intervillous space. It is drained by veins through which fluid can readily escape. All the other cavities are closed and filled with

fluid. Many years ago Bremer described in the human placenta regions in which the tropho-
blast was reduced to an extremely fine film (in histologic preparations) with the capillaries
very close to the intervillous space. It may be of course that they serve to eliminate the
amniotic fluid absorbed by the fetus. The short extent of the capillaries which Dr. Reid has
demonstrated may be significant physiologically.

It is interesting that in Boston, where a new epoch has been initiated in human
embryology by Hertig and Rock, we have also eminent students of the physiologic anatomy
of the placenta.

DR. REID (Closing).—Briefly, there are two remarks that we should like to make.
Dr. Bartelmez mentioned Dr. Bremer's work. On the basis of Dr. Bremer's observations the
idea was considered that the arrangement of the vessels within the terminal villi on the fetal
side was such that they might function as an excretory organ. The arterioles and terminal
capillaries being in close proximity to the trophoblast layer might present a similar arrange-
ment as that which occurs in the glomerulus. From our observations to date, however, such
an arrangement does not appear to be the case. Finally, I should like to give credit to Dr.
Seymour L. Romney, who did the major part of this work.

ENDOMETRIOSIS, CLINICAL ASPECTS AND THERAPEUTIC CONSIDERATIONS*†

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SINCE Sampson[1] published his classic study of endometriosis in 1921, intensified interest in the disease is evidenced by the accumulated literature regarding its protean manifestations, obscure etiology, pathologic vagaries, bizarre symptomatology, unpredictable course, and capricious response to the therapeutic measures advocated. The contributions of Goodall,[2] Meigs,[3] Counseller,[4] Novak,[5] Fallon,[6] Holmes,[7] and others present divergent and controversial views on these points. In the absence of precise knowledge of its pathogenesis, no final conclusion can be drawn that the responsible factor is implantation, or abnormal celomic metaplastic changes, or—as Halban[8] suggests—lymphatic transplantation incidents. Each theory fits some cases, but none is generally applicable.

Emdometriosis presents two distinct characteristics: (1) a foreign invasion of the endometrial cells; and (2) destruction of hemorrhagic extravasations of the menstrual cycle and subsequent formation of blueberry and tarry cysts and adhesions. The resulting pathologic sequelae and symptomatology depend upon the mode of spread of the disease and the response to ovarian hormones. Endometriosis exhibits some of the properties and propensities of new growths and sequelae similar to those of inflammatory affections.

Clinical Data

The analysis here made comprises 88 operative and histologically proved and 74 clinical cases taken from a series of 2,000 consective private patients with varied gynecological complaints. The objective is to correlate this material with the prospects for symptomatic relief and the attainment of fertility.

The diagnosis of endometriosis was made 162 times, corresponding to an incidence of 8 per cent. In contrast, only 8 of 3,563 gynecological cases on the ward service of Kings County Hospital during 1949 were diagnosed as endometriosis, an incidence of but 0.22 per cent.[9] Though these statistics are derived from too small a series to allow positive evaluation, they seem to coincide generally with the ratios in extensive data collected by others, indicating that endometriosis occurs more often in private than in ward patients. The explanation has been offered that in the so-called upper classes of society the marriages are likely to occur late and pregnancies are thus postponed, so that there are many recurrent menstrual cycles in which hormonal reactions stimulate the celomic cells to produce Müllerian growths. But there are many variants which are more dynamic than fixed, and these do not support class distinctions in a comparison

of private and ward patients. The mass of data produced by Welpton and Kiser,[10] the 1949 census reports, and other evidences conclusively contradict the theory that general decline in birth rate is associated with biologic deterioration.

In the present series, 59 of the 88 operative cases and all of the 74 suspected clinical cases were primarily infertility problems. A complete fertility survey, in both the male and the female, was always made. All of the cases were followed up, either by personal observation, or by questionnaires completed by the patients themselves.

Tubal patency is usual in endometriosis; there were only four cases of bilateral and eleven of unilateral occlusion. One of the bilateral cases was a true endometriosis; in both tubes the mucosa had been replaced by endometrial tissue. We noticed no exacerbation or increase of endometriosis which could be attributed to repeated tubal insufflation or hysterosalpingography. Adhesions of the ovary, which are frequent in endometriosis, may at the time of ovulation prevent the rotation of the ovary on its ligament toward the infundibulum for the reception of the ovum, and thus cause fertilization failure.

Age Incidence

Of the 67 operatively proved external endometriosis cases, 6 (or 8.9 per cent) were in the 21 to 25 year age group; 10 (or 15 per cent) in the 26 to 30 group; 43 (or 64.4 per cent) in the 31 to 40 group; and the remaining 8 (or 11.7 per cent) in the 41 to 60 year group.

Of the 74 clinically suspected external endometriosis cases, 2 (or 2.7 per cent) were in the 15 to 20 year age group; 6 (or 8.1 per cent) were in the 21 to 25 group; 36 (or 48.7 per cent) were in the 26 to 30 group; 24 or 32.4 per cent) were in the 31 to 35 group; and the remaining 6 (or 8.1 per cent) were between the ages of 36 to 40; there were no older subjects among these clinically suspected external cases.

There were 21 cases of internal endometriosis, divided as follows: 2 (9.5 per cent) in the 31 to 35 year age group; 6 (28.5 per cent) in the 36 to 40 group; 10 (47.6 per cent) in the 41 to 45 group; 2 (9.5 per cent) in the 46 to 50 group; and 1 (4.7 per cent) in the 51 to 55 group.

It is of interest that in the operatively proved group only 16 (or 23 per cent) were less than 30 years old, and that 48 (or 71 per cent) were 31 to 40 years old, indicating the inclination to allow younger women to carry on with their disability if it is not too incapacitating. The fact that the clinicallly suspect cases show a higher incidence in the younger bracket may be attributed to the fact that they represent an early stage of endometriosis diagnosed in infertility examinations, in which it was hoped that the patients would become pregnant before it became necessary to intervene surgically. Patients in the older group who were treated surgically had pelvic lesions in addition to endometriosis. After the menopause, endometriosis becomes only an asymptomatic relic.

Symptomatology

In conjunction with the usual diagnostic procedures, palpation, hysterography, culdoscopy, laparotomy, the histories of the patients were taken carefully and methodically, so as to exclude pelvic inflammations caused by antecedent gonorrheal, tuberculous, or postpartum infections, which may present similar symptoms and stigmas. The symptomatology in the series is reproduced is Table I.

Absence of dysmenorrhea in a significant number of cases of endometriosis has been noted by other investigators.

Menorrhagia was a frequent symptom in all types; metrorrhagia was generally encountered as an irregular intermenstrual spotting. In some cases the

menstrual abnormalities were not due to any gross pathological changes in the ovaries, but were due to associated fibroids or cystic hyperplasia of the endometrium, and in others it may have been connected with some endocrine imbalance. Endometrial biopsies, taken in all of the cases incidental to infertility investigations and in some others at the time of bleeding, revealed endometria of bizarre architecture in all phases of the menstrual cycle. There were, however, only six cases of the persistent anovulatory type.

TABLE I. SYMPTOMATOLOGY

SYMPTOMS	EXTERNAL ENDOMETRIOSIS				INTERNAL ENDOMETRIOSIS	
	OPERATIVELY PROVED		CLINICALLY SUSPECTED			
Dysmenorrhea	51	76.1%	63	85.1%	6	28.5%
Menorrhagia	34	51.7%	49	66.2%	12	57.1%
Metrorrhagia	29	43.2%	24	32.4%	14	66.6%
Low abdominal pain	28	41.7%	31	41.8%	7	33.3%
Backache	25	37.3%	26	35.1%	2	9.5%
Dyspareunia	16	23.8%	11	14.8%	2	9.5%
Headache	4	5.6%	0		0	
Rectal discomfort	9	13.4%	10	13.5%	2	9.5%
Bladder symptoms	5	7.4%	0		2	9.5%
Nausea and vomiting	4	5.6%	0		0	
Amenorrhea	1	1.4%	0		1	4.7%

In one-third of the cases with lower abdominal pain in the operatively proved external endometriosis group, the pain was aggravated during menses, jarring of the pelvis, intercourse, pelvic examination, standing for a long time. Pain was not relieved by antispasmodics or heat. Backache, sacral in location, dyspareunia, and rectal discomfort, particularly at menstruation, occurred relatively frequently. In no case were there symptoms of an acute abdominal crisis resulting from sudden rupture of an endometrial cyst. There was one instance

TABLE II. CONSERVATIVE OPERATIONS, WOMEN UNDER 40 YEARS

(Percentages based on total number of cases)

OPERATIONS	NO. CASES	RELIEF OF SYMPTOMS			SUBSEQUENT PREGNANCY
		COMPLETE	PARTIAL	FAILURE	
Suspension of uterus, section of ovary Presacral neurectomy Resection of ovary	9	5 (15.6%)	1 (6.2%)	3 (6.2%)	2 (6.2%)
Fulguration of implant Resection of ovary	6	3 (9.3%)	2 (6.2%)	1 (3.1%)	1 (3.1%)
Presacral and ovarian neurectomy Resection of ovary, myomectomy	6	3 (9.3%)	3 (9.3%)		2 (6.2%)
Suspension of uterus, fulguration of implants	4	2 (6.2%)	1 (3.1%)	1 (3.1%)	2 (6.2%)
Salpingo-oophorectomy, unilateral Suspension of uterus, unilateral Salpingo-oophorectomy	2	2 (6.2%)			1 (3.1%)
Suspension of uterus, unilateral Salpingo-oophorectomy	2	2 (6.2%)			0
Fulguration of implants Resection of ovary	2	1 (3.1%)	1 (3.1%)		1 (3.1%)
Salpingo-oophorectomy, unilateral	1	1 (3.1%)			0
Total	32	19 (59%)	8 (25%)	5 (15%)	9 (28%)

of intestinal obstruction from endometrial ectopia, a comparatively rare but important symptom because of its confusion with bowel carcinoma.

There seemed to be no relationship, in an analysis of the symptomatology, between the frequency and severity of the symptoms, the nature and location of the ectopia, and the relief of the condition following operation in each of the three groups.

The nature of the operations, the effects on the symptoms, and the subsequent pregnancies are summarized in Table II.

Duration of Childlessness

It is problematical what part endometriosis plays in the high incidence of infertility, ranging from 34 to 100 per cent.[11] There is evidence that the development of endometriosis is favored in childlessness, but pregnancy with endometriosis does occur. Data accumulated by demographers and sociologists indicate a substantial inverse ratio between the socioeconomic status and the progeny, almost entirely due to group differences and the effectiveness and prevalence of contraceptive procedures. Moreover, in numerous cases, an unsuspected sterility is masked by the use of contraception, and the actual existence of the inadequacy for reproduction is recognized only when a couple decide that they now want to have children. In their Indianapolis study of 1937, Welpton and Kiser[10] estimated that impairment of fertility had reduced the average ability of all couples for procreation to 27.4 per cent below normal.

In the analysis herewith presented, 142 (88 per cent) of the women had used contraceptives, and 78 of them (48 per cent) had done so for more than a year prior to their initial examinations. This may indicate that possibly the deliberate avoidance of pregnancy had favored the development of endometriosis. In the 67 external operative cases of endometriosis, 45 patients had been childless for five years, 10 for between 3 and 5 years, eight between 1 and 3 years, and four less than 1 year. In the 74 suspected cases, the figures are, respectively, 30, 26, 16, and 2. In the 21 internal cases, 16 patients had been childless for more than 5 years, and the others between 3 and 5 years.

The average marriage ages for the external operative, clinically suspected, and internal cases were, respectively, 23, 20.6, and 24 years. The 1940 census showed that at that time there were married 12 per cent of women between 15 and 19 years of age, 53 per cent between 20 and 24, and 91 per cent over 45. The greatest fecundity rate was in women between 20 and 25 years. Apparently, the marriage ages of our endometriosis patients were relatively no higher. No final conclusions, however, can be drawn. In every other country of the Western world which has available census statistics, the marriage age is lower than that in the United States, and to know the incidence of endometriosis in these countries would be extremely interesting. Beacham[12] reported that endometriosis is rare in China, India, and the Orient, where marriages occur very early in life.

Number of Children

In the external operative group, 31 (46.2 per cent) were nulliparas; 21 (31.4 per cent) had one child; 10 (15 per cent) had two children; 3 (4.5 per cent) had three children; and 2 (2.9 per cent) had more than three children.

In the clinically suspected group, 62 (83.6 per cent) were nulliparas; and 12 (16.4 per cent) had one child.

In the internal group, 7 (33.3 per cent) were nulliparas; 2 (9.5 per cent) had one child; 7 (33.3 per cent) had two children; 3 (14.2 per cent) had three children; and 2 (9.5 per cent) had more than three children.

In the clinically suspected cases, the low incidence of childlessness for more than 5 years was due to the fact that the group consisted of young women, many of whom had not been married for that length of time.

Sixteen (76 per cent) of the patients with adenomyomas had been infertile for more than 5 years. Although adenomyomas were found in seven of the nulliparas in this group, women with diffuse myomas do as a rule have children. Thus trauma may be the cause of invasion of the myometrium by the endometrial cells, with subsequent enlargement of the uterus and progressive dysmenorrhea.

Physical Diagnosis

The typical shotty cul-de-sac pathognomonic of endometriosis was found in 46 (68 per cent) of the operative external cases and in 58 (78 per cent) of the clinically suspected cases. Fixed retroplacement of the uterus was encountered in 21 (31 per cent) and 24 (32 per cent), respectively. Palpably enlarged ovaries, tender adnexa, and uterine enlargement were frequent findings in the external cases. The uterine enlargements were almost invariably due to coexistent fibromyomas of the uterus, excepting in the internal cases, where fibromyomas and adenomyosis were the causative factors.

Distribution

The most frequent sites in the operatively proved cases of this series were the ovary (51 times), the posterior cul-de-sac (38 times), and the rectosigmoid (11 times). Six of the external cases showed a concomitant adenomyosis. The serosal surface of the uterus was implicated in 9 of the cases.

Associated Conditions

The most frequent associated findings were myomas and retrodisplacement, but it is a matter of speculation whether either of these predisposes to the development of endometriosis, in view of the fact that 20 per cent of otherwise normal

TABLE III. ASSOCIATED CONDITIONS

CONDITION	EXTERNAL ENDOMETRIOSIS				INTERNAL ENDOMETRIOSIS 21	
	OPERATIVELY PROVED, 67		CLINICALLY SUSPECTED, 74			
Fibromas of the uterus	21	31.3%	15	20.2%	15	71.4%
Myometrial hypertrophy	13	19.4%	0		0	
Endometrial hyperplasia	19	28.3%	0		1	4.7%
Uterine retrodisplacement	21	31.3%	36	48.6%	0	
Adenocarcinoma of fundus	2	2.9%	0		0	
Follicular cysts of ovary	26	38.8%	6	8.1%	8	38%
Dermoid cyst of ovary	1	1.4%	0		1	4.7%
Corpus luteum cysts of ovary	8	11.9%	0		0	
Simple cysts of ovary	6	8.9%	0		0	
Hemorrhagic cysts of ovary	2	2.9%	0		0	
Serous cystadenoma of ovary	1	1.4%	0		0	
Perioophoritis	2	2.9%	0		0	
Chronic salpingitis	4	5.9%	4	5.4%	1	4.7%
Pyosalpinx	0		0		1	4.7%
Adenomyosis	6	8.9%	0		21	100%
Uterus didelphys with hematometra of right uterus	1	1.4%	0		0	
Acute appendicitis	1	1.4%	0		0	
Uterine prolapse	0		0		3	14.2%
Endometrial polyp	1	1.4%	0		0	
Cervical polyp	1	1.4%	0		0	
Pregnancy	0		0		1	4.7%
Cystorectocele	0		0		3	14.2%
Intestinal obstruction (sigmoid)	1	1.4%	0		0	

mature women have uterine myomas, and 20 per cent of otherwise normal women have uterine displacements. We have never observed menstrual fluid exuding from the fimbriated ends of the tubes during operation.

The nature and number of the associated conditions are enumerated in Table III.

The listings under "Clinically Suspected Cases" represent a reasonable degree of certainty. Adenocarcinoma of the fundus uteri was found in 2 of the 67 cases of external endometriosis, and in both there was an associated adenomyosis. In neither, however, was it possible to prove the development of carcinoma from the uterine endometrial ectopia. Sampson[1] and others have observed cases in which the carcinoma developed from the epithelium in the endometrial cysts. But Wharton[13] stated that malignant change is unusual, Holmes[7] failed to find a single carcinoma in his series, and Counseller[4] saw only one in his 308 cases, so that our incidence was probably fortuitous.

Treatment

Opinion is now well crystallized that general prophylaxis—early marriage, frequent childbearing, balanced diet, dilatation of the cervix for stenosis, meticulous care in instrumentation—will materially reduce endometriosis incidence. Many cases require no active treatment at all, and when definitive therapy is indicated our first line of endeavor is medical or conservative surgical, rather than radical.

Medication with thyroid given empirically, and with androgens and estrogens used judiciously, was effectual in a number of our cases. Androgens were of only temporary value, because large doses were usually needed. To avoid possible masculinization, more than 400 mg. were not given, and administration was intermittent. The patients under hormone treatment were all young and exhibited minimal pathological changes definitely related to the menstrual cycle; our aim, of course, was to avoid surgical procedures whenever possible. Androgens were also used in a number of postoperative cases, and temporarily the disease process became quiescent, both locally and generally.

Complete relief in this group was obtained in seven cases (15 per cent), and in four of them (10 per cent) pregnancy occurred. The average time between beginning of treatment and delivery was 5.3 years. In thirty-three (72 per cent) there was failure, and these were subsequently carried along with residual symptoms treated with sedatives, antispasmodics, and benzedrine. The results in this group of cases are shown in Table IV.

TABLE IV.   RELIEF OF SYMPTOMS, PALLIATIVE TREATMENT

CLINICALLY SUSPECTED CASES			PREGNANCY	
Complete relief*	8	15%	5	10%
Partial relief	6	13%	3	6%
Failure†	33	72%		
Total	47	10%	8	16%

*One case treated by diethylstilbestrol with one pregnancy.
†Five were treated with diethylstilbestrol 3 to 8½ months.

Karnaky[14] has reported distinctly favorable results in endometriosis from large doses of diethylstilbestrol; 5 of his 37 patients became pregnant. We have followed his treatment in 11 cases. Four of these were previously scheduled for operation and in these there was no local or general improvement under stilbestrol; in one cases, 2,500 c.c. of blood had to be given prior to operation because of severe hemorrhage following use of the drug. The remaining 6 of these 11 were clinically suspected cases of endometriosis, and had failed to respond to

androgens. One patient became pregnant after use of stilbestrol for one year. In two there was definite lessening of induration in the posterior cul-de-sac. Four became amenorrheic. One, after seven months of stilbestrol, is now menstruating regularly with practically no discomfort, and her basal temperature, previously monophasic, now shows normal biphasic response. Whether or not the symptoms will recur and any further pregnancies will result, is unpredictable. Stilbestrol was not used in cancer suspects or in patients with cystic ovaries more than 5 cm. in diameter.

The modus operandi of prolonged and increased use of diethylstilbestrol has been explained as having a suppressing effect on the anterior pituitary, thus inhibiting or diminishing ovarian activity and causing atrophy of the ovaries, which in turn reduces estrogenic stimulation to the normally placed or ectopic endometrium, with resulting amenorrhea. Small doses, even though continuously used, do not produce this effect. The same phenomenon probably occurs during pregnancy. To explain why, with stilbestrol therapy, endometrial lesions undergo atrophy while the intrauterine endometrium undergoes hyperplasia, Greenblatt[15] postulated that endometriosis may in most cases be derived from celomic epithelium or some other embryonic cells which are easily destroyed by large and continuous doses of estrogen. However, at present the mode of action of stilbestrol can only be conjectured, *and its use should be cautiously and judiciously individualized.*

Radical operation and x-ray or radium irradiation are last resorts, because endometriosis is frequently of clinical import in relatively young persons in whom ovarian and gestational functions should, if possible, be conserved. Sterilization and menopause may render the cure worse than the disease. The patient's age, the nature and extent of the lesions, and her neurologic make-up are primary considerations. Young women, particularly if they desire children, should be conservatively treated even if a resection for intestinal endometriosis is necessary to avoid sacrificing ovarian function. Prior to conservative procedure, the possibility that later reoperation or irradiation may be necessary, and the reasons why this calculated risk should be assumed, must be fully explained to the patient or her family.

Pregnancy has been reported in as little as 2 per cent to as much as 83 per cent[16] of endometriosis patients who had undergone conservative surgery. The preservation of only a small fragment of functionating ovarian tissue may suffice to permit gestation. In conservate operations we usually perform presacral neurectomy so as to cure the existing dysmenorrhea and as a safeguard against subsequent development of this trouble. This procedure is of value if the endometriotic lesions are confined to the uterus, uterosacral ligament, and vesical tissues. However, pain resulting from implants involving the broad ligament, ovaries, or other pelvic structures is not relieved thereby, and in these instances we include sectioning of the ovarian nerves. It should be remembered that these nerves can regenerate completely within three to five years, and may have their sensitivity restored.[4] Thorough exploration and adequate resection of the involved and suspected tissues are equally important if the patient is to be relieved. Excision, high frequency current, or carbolization is used to destroy peritoneal implants.

By adhering to these principles, the results of conservative surgery have been gratifying, reoperation for exacerbation of symptoms having been required in only 5 or 6 per cent of our cases. Meigs[3] reported 9 to 26 per cent of reoperations in the cases reviewed by him.

In women over 40 years of age, there is no hesitancy about radical surgery. The menopausal symptoms that follow castration in endometriosis are not as severe as those following castration for other reasons. This may be explained by the fact that the patient with endometriosis has already bordered on menopause

at the time of the operation because of the gradual destruction of ovarian tissue, and hence could adjust herself more easily. A panhysterectomy should be performed whenever possible. At times advanced endometriosis with a frozen pelvis and rectal or other contiguous visceral involvements may be encountered. In such instances, supravaginal hysterectomy with bilateral salpingo-oophorectomy preceded by ureteral catheterization is the procedure of choice. Few conditions demand more surgical skill and judgment. At times the endometriosis may be so extensive as to permit only bilateral oophorectomy or closure of the abdomen with subsequent irradiation, plus hormonal therapy. As a rule we do not favor irradiation as the initial method of treatment, because surgery makes possible the correction of associated pathological developments common in older groups and the preservation of ovarian function in younger subjects. Castration has an effect upon skin, bone, and hair[3] and should be avoided if possible, particularly in young women.

TABLE V. TREATMENT

PROCEDURE	EXTERNAL ENDOMETRIOSIS		PREGNANCY		INTERNAL ENDOMETRIOSIS	
Complete hysterectomy, bilateral-salpingo-oophorectomy	26	58.8%			6	28%
Subtotal hysterectomy, unilateral salpingo-oophorectomy	4	5.9%			4	19%
Complete hysterectomy	2	2.9%			8	38%
Vaginal hysterectomy	0				3	14.2%
Salpingo-oophorectomy, bilateral	1	1.4%			0	
Oophorectomy, bilateral	1	1.4%			0	
Suspension of uterus, resection of ovary, presacral neurectomy	9.	13.4%	2	6.2%	0	
Resection of ovaries fulguration of implants	6	8.9%	1	3.1%	0	
Resection of ovary, presacral and ovarian neurectomy	6	8.9%	2	6.2%	0	
Resection of ovary, suspension of uterus, myomectomy, removal of implants	4	5.9%	2	6.2%	0	
Salpingo-oophorectomy, unilateral	2	2.9%	1	3.1%	0	
Suspension of uterus, unilateral salpingo-oophorectomy	2	2.9%			0	
Suspension of uterus, unilateral salpingo-oophorectomy fulguration of implants	2	2.9%	1	3.1%	0	
Resection of ovary, salpingo-oophorectomy unilateral	1	1.4%			0	
Abdominal hysterectomy, bilateral salpingo-oophorectomy, resection of colon	1	1.4%			0	
Total	67	100%	9	28%	21	100%

We have been impressed by the finding that at times hysterectomy without oophorectomy prevented progression of small endometrial implants. Even though the ovaries are left and functioning and the patient does not menstruate, the remaining implants stay relatively quiescent. This is probably similar to the action of metastases following the removal of the original growth in malignancy.

The diagnosis of endometriosis, of course, does not demand immediate surgical intervention. Watchful waiting and careful observation subject the patient to no hazard, and many cases respond to medical treatment. As in other fields of medicine, spontaneous remission of symptoms may occur. In the clinically suspected group, 9 instances of conception occurred without therapeusis, despite defects recognized as expressions of endometriosis. Many young women, once

assured that no serious consequences will result from deferring operation, may prefer to endure the discomforts of moderate dysmenorrhea for five to seven days in a month and relieve them with palliative measures, rather than run the risk of surgical treatment. In our series, 18 of the clinically suspected cases are receiving no active therapy despite persistence of symptoms. In these cases surgery is indicated only when nonsurgical means fail to halt progressive dysmenorrhea, progressively increasing low abdominal or rectal pain, dyspareunia, menorrhagia, or metrorrhagia. Forty-seven (63 per cent) of the clinically suspected cases are being treated palliatively. Patient medical treatment of mild endometriosis was rewarded by pregnancy in 8 cases (16 per cent). Three however, have subsequently aborted. The surgical treatment employed in these cases of endometriosis is set forth in Table V.

Hysterectomy of one type or another was performed in all cases of external endometriosis, this being the procedure of choice when operation is required. Castration was required in 28 (42 per cent) of the external endometriosis group, and hysterectomy in 32 (47 per cent). Treatment sufficiently conservative to preserve both menstrual and gestational functions was given in 32 (47 per cent) of the group.

A synopsis of the results in the three groups which comprise our series of cases is given in Table VI.

TABLE VI. RESULTS

NO. OF CASES		COMPLETE RELIEF		PARTIAL RELIEF		FAILURE		PREGNANCY	
Total operated upon	88	75	85%	8	9%	5	5 plus %	9	10%
Conservative operation on patients under 40 years	32	19	59%	8	25%	5	15%	9	28%
Clinically suspected cases	74	17	23%	6	8%	51	69%	17	23%
Treated	47	8	15%	6	13%	33	72%	8	16%
Untreated	27	9	33%			18	67%	9	33%

There was no operative mortality in this series.

These data do not seem to indicate any correlation between the amount and location of endometriosis, the postoperative relief, and subsequent pregnancy in the patients conservatively operated upon. It may be inferred that the presence of a considerable amount of endometriosis is no contraindication, from the viewpoint of prognosis, for conservative surgery. These observations appear to be in agreement with those of Bacon.[16]

These data permit the further inference that surgery in younger women may be deferred until symptoms have become progressively more severe. As pain has a relative threshold and is a variable factor in each person, discrimination and individualization must determine the necessity for surgery in these cases. In a limited number of cases, amelioration of the symptoms and subsequent pregnancy occur with or without treatment.

Summary and Conclusions

1. In the series here reported, approximately 80 per cent of the patients with external endometriosis were in age groups of 26 to 40 years, and approximately 75 per cent of those with internal cases were in the age groups of 36 to 45 years.

2. The symptoms in all groups were manifold, the most common being a characteristically progressive dysmenorrhea, menstrual abnormalities, and low abdominal pain.

3. The most frequent physical findings were cul-de-sac tenderness and irregularity, palpably enlarged ovaries, tender adnexa with or without induration, and uterine enlargement almost invariably due to coexisting fibromas.

4. Prolonged childlessness was frequent in all types. The patients generally gave a history of long use of contraception and this may indicate that endometrial lesions may be caused by deficiency of endocrines which are normally produced during pregnancy. Accordingly, early marriage and frequent childbearing may be regarded as prophylactic factors. However, endometriosis may develop despite previous pregnancies, and women with no signs of endometriosis may be sterile.

5. Treatment was preferably expectant and conservative, especially in young women, with a view to preserving ovarian and gestational functions.

6. Surgery was resorted to only when symptoms were uncontrollably progressive in the younger groups; in older women there was no hesitancy about radical procedures.

7. There appeared to be no significant differences in the number of pregnancies resulting from conservative surgery, palliative therapy, or no therapy in women in the same age groups.

8. There was no correlation between prognosis and the amount and location of endometrial lesions, the postoperative symptomatic relief, and subsequent pregnancies.

9. Group studies supply no definite and fixed rules for individual cases.

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AN ANALYSIS OF TEN YEARS OF CESAREAN SECTION AT THE CINCINNATI GENERAL HOSPITAL

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RECENT trends in the use of the cesarean section operation to alleviate obstetrical difficulties have been studied by numerous authors[1-5] during the past five years. All have noted a steady increase in incidence, broadening of indication, with decreasing fetal and maternal mortality. This change in attitude appears to coincide with the appearance of freely available antibiotics, chemotherapy, widespread development of blood banks, improvement in surgical technique, better regional anesthesia, and the increasing use of the extra-peritoneal approach. D'Esopo[1] noted that, in 1948, 70 per cent of the total operative deliveries at the Sloane Hospital were cesarean sections. This connotes a steady decrease in the number of difficult vaginal deliveries and this substitution has been accomplished with an extremely low maternal mortality rate. No maternal deaths occurred in 1,064 consecutive cesarean sections.

D'Esopo[1] further speculates that at some future time all potentially difficult operative deliveries may be by section and only "easy" deliveries will be handled vaginally. Normal vaginal delivery will always be safer than delivery by section, and the items listed above make vaginal delivery even safer. If, however, it can be shown that the maternal risk in cesarean section is not greater than in difficult vaginal operations, and the fetal mortality and fetal trauma are less by this method, then a general acceptance of this concept may be forthcoming. For the past nine years at the Sloane Hospital delivery by section has not been more hazardous for the mother than by vaginal operation, low forceps excluded.

In an effort to compare the present status of cesarean section in this institution with that of other large teaching hospitals and to determine the relative maternal and fetal risks, this study was carried out. The results form the object of this paper.

Material

The material included in this analysis was collected from the obstetric records of the Cincinnati General Hospital. It covered a 10 year period from 1940 to 1949, inclusive. During this time 251 cesarean sections were performed. Of these, 189 were done by the resident staff and 62 by the attending staff. There is no patient selection in this hospital. The majority of cases are registered early in the prenatal period, but booking is done only on a financial basis and there is no "routing" of abnormal cases. There is no private service, all patients being under the direct care of the resident staff.

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Admittedly, the total number of cases is small. However, in this institution, where for many years an incidence of approximately 0.7 per cent existed, a doubling of incidence, extension of indication, change of anesthesia, and lowering of fetal mortality rate have occurred. The rationale stimulating this change is of interest.

Incidence

The incidence is shown in Fig. 1. There has been a slow but gradual rise from 0.7 per cent in 1940 to 1.5 per cent in 1949. This low incidence during the first 8 years of the report reflects an extremely conservative approach in which practically all of the operations were done for cephalopelvic disproportion. Placenta previa, abruptio placentae, uterine inertia, and necessary inductions of labor were handled during this period by the hydrostatic bag. In 1948 a revision of departmental policy was formulated, exemplified by the doubling of incidence during that year. The over-all incidence of 1.0 per cent for the 10 year period remains low considering the high percentage of Negro patients cared for in this institution.
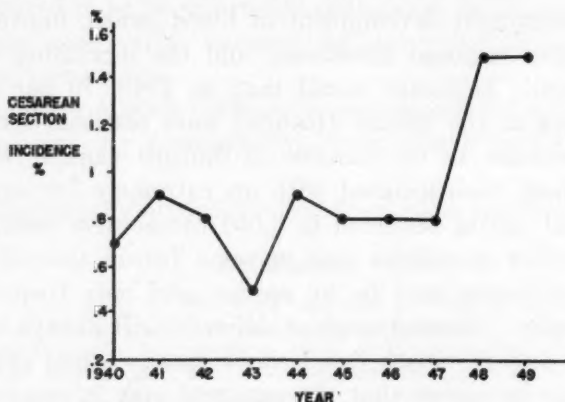
Fig. 1.—Incidence of cesarean section, 1940-1949.

Table I lists the cesarean section incidence in 10 of the major teaching clinics of the country. The average incidence is 5 times as high as that of the Cincinnati General Hospital. A further analysis of the 4 major private hospitals in this city reveals incidence rates varying from 1.3 per cent to 2.6 per cent and an average rate of 1.8 per cent. The slight but definite increased incidence in the private hospitals parallels the difference noted by many authors between private and ward case incidence.

Hennessy[2] noted that in his clinic the incidence in private cases was 5.82 per cent against 1.75 per cent for service cases. McCormick[3] found the ratio to be 8.80 per cent private and 2.80 per cent service. Is there justification for this marked difference? Do social position and income bracket influence the decision of the obstetrician? Is a greater premium placed on fetal life in private patients? Should fetal life be jeopardized and maternal soft parts traumatized and prolonged labor condoned so that interns and residents may, by trial and error, observe and commit obstetrical mistakes as part of a recognized teaching program?

The answers to these questions may be obtained only by a study of a large series of cases plotting fetal mortality and fetal salvage rate against cesarean section and operative delivery. D'Esopo[1] has recently presented excellent statistical material in this regard.

TABLE I. CESAREAN SECTION RATES

New Haven Hospital		5.9%
Margaret Hague		2.6%
Chicago Lying-in		5.5%
New York Hospital		2.1%
Boston City Hospital		4.2%
Kansas City		7.1%
Johns Hopkins Hospital		5.5%
Cleveland Maternity		6.1%
Philadelphia Lying-In		5.8%
Sloane Hospital		5.8%
Average	4.9%	
Cincinnati—Bethesda (1940-1949)		1.3%
Cincinnati—Christ (1940-1949)		1.6%
Cincinnati—Good Samaritan (1940-1949)		1.8%
Cincinnati—Jewish (1940-1949)		2.6%
Average	1.8%	
Cincinnati General (1940-1949)		1.0%

What should the incidence of cesarean section in a teaching clinic be? McCormick[3] found the average incidence in 20 major clinics during the years 1940 to 1945 to be 3.32 per cent. This comprised 8,118 sections in 244,369 deliveries, and would seem to be a generally accepted figure by most obstetricians. Cron[4] has stated, however, that he considers an incidence of 5.0 to 5.5 per cent to be the irreducible minimum. He feels that a rate lower than that will produce a higher stillbirth and neonatal death rate and will result in severe, and sometimes irreparable, damage to maternal soft parts.

The phrase "obstetric cripple" should be analyzed while incidence is being surveyed. This term, as it is now loosely used, describes the patient who has had the "unfortunate" experience of having had a cesarean section some time in the past. She then becomes a patient of particular importance with subsequent pregnancies and is looked upon with foreboding because of potential uterine rupture. Actually what are the chances of uterine rupture for this patient?

Brierton,[6] in a recent survey of 246 patients who carried pregnancies to the last trimester after a previous cesarean, concluded: (1) In the present-day hospital practice, rupture of the pregnant uterus occurs once in 2,000 deliveries. Approximately one-half of these will be ruptures of the scars of previous sections. (2) About 3 per cent of cesarean scars will rupture in subsequent pregnancies and classical scars are more than twice as likely to rupture as low flap scars.

It may be concluded from this study that uterine rupture from a previous cesarean section scar may be expected once in 4,000 deliveries and in about 1 to 1.5 per cent of low flap cases. The peak incidence will be during the last 4 weeks of gestation and during this time these patients should have close observation and early operative intervention with the appearance of abdominal pain or tenderness.

After perusal of these data can it then be said that the patient with a well-healed low cervical scar is more of an "obstetric cripple" than the young primipara who, because of soft part trauma from a difficult forceps delivery, has developed a fistula, cystorectocele, third degree lacerations, vaginal and cervical adhesions with scarring, and who must necessarily have later plastic operations performed?

Race, Age, and Parity

Table II shows that over twice as many sections were performed on Negro patients (68 per cent Negro, 32 per cent white). That this is not due to an in-

creased number of Negro patients is shown by the fact that only 0.7 per cent of all white patients were sectioned whereas the incidence in the Negro group was 1.3 per cent.

The average age was 24 years.

Fifty-three per cent of the operations were performed on multiparas and 47 per cent on primigravidas. There were only 8 sections on elderly (over 35 years of age) primigravidas.

TABLE II. RACE AND AGE

	NUMBER	PER CENT	INCIDENCE
White	82	32	.7%
Negro	169	68	1.3%
		NUMBER	PER CENT
Age (years)	10-19	75	29
	20-29	122	48
	30-39	50 ⎱	23
	40+	4 ⎰	

Indications

Fig. 2 outlines the various primary indications for the operation. The majority of operations, as in most studies, were done for cephalopelvic disproportion and as repeat sections (185 cases). Hemorrhage (placenta previa and abruptio placentae) necessitated 31 operations and pre-eclampsia 8.

Disproportion.—It is evident that in the early part of the decade almost all of the operations were for disproportion plus a few repeats. There were no sections performed for "absolute" disproportion (conjugate vera of 7.5 cm. or less).

In 61 cases the operation was performed purely on the basis of the x-ray and pelvic examination, whereas 67 patients were submitted to a trial of labor. The present policy in cases of relative disproportion is to allow labor to begin spontaneously and a period of 6 to 8 hours of observation to be carried out. Prophylactic antibiotics and chemotherapy, intravenous fluids, and sedation are administered. Repeated x-ray pelvimetry during this period is advised. Sterile vaginal examinations are performed at selected intervals. If progress is good, in the absence of fetal distress, the membranes may be ruptured and an additional 4 to 6 hours of labor permitted. If progress is poor, or if uterine inertia is superimposed, or there is fetal distress, laparotrachelotomy is performed.

Repeat Sections.—Fifty-seven operations were performed in this group. Five patients were already in labor when the procedure was begun and in one instance incomplete uterine rupture was discovered. In general, it is the policy of the clinic to do repeat sections a week or 10 days prior to the estimated date of confinement on all patients who were previously sectioned for disproportion or who have classical scars or a history of a febrile puerperium. Patients who have had previous low flap sections with normal puerperia, when the indication was hemorrhage, toxemia, or malpresentation, are hospitalized near term and x-rays and careful pelvic examination carried out. Each case is considered as a separate problem and a decision is made after surveying the presenting part, its station, position, fetal size, and the character of the cervix. During labor the type of contractions and the progress and facility of cervical effacement and dilatation are closely observed and in the presence of any abnormality section is done.

Hemorrhage.—During the past 10 years 17 cases of placenta previa and 14 cases of abruptio placentae were handled by means of cesarean section. During this period the incidence of cesarean section as a method of treatment for placenta previa was 14 per cent. In contrast, D'Esopo[1] noted that from 1934 to 1943 his incidence averaged 30 per cent and that it now has leveled off at about 75 per cent. A definite trend toward the use of abdominal delivery in hemorrhage has been noted in the last 3 years. Fig. 2 demonstrates that 23 of these 31 sections have been done during the 1947-1949 interval.

In the past the hydrostatic bag was utilized frequently in this clinic for all degrees of previa, including certain cases of the complete type. A recent analysis[7] of the fetal mortality rate in 60 cases of placenta previa during the years 1940-1949 handled with the hydrostatic bag in the Cincinnati General Hospital revealed the fetal mortality rate to be 50 per cent gross and 37 per cent corrected. At the present time minimal degrees of placenta previa, with an amenable cervix, are handled by simple rupture of the membranes and spontaneous delivery. The more severe cases are treated by cesarean section and all uteri are packed before closure.
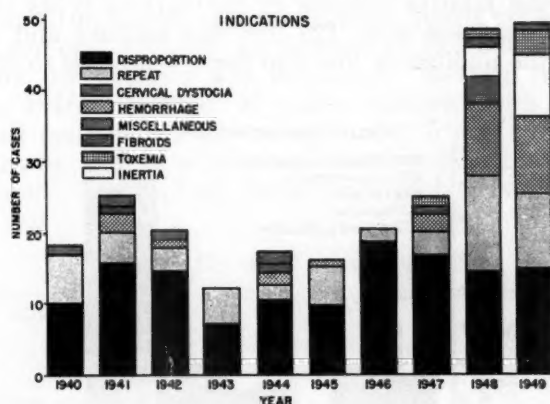
Fig. 2.—Indications for cesarean section, 1940-1949.

The approach to emptying the uterus in cases of abruptio placentae has also changed. In this condition it is of importance that the uterine contents be evacuated by the most expedient means and with the least trauma to the mother. If this can be accomplished vaginally, by simple rupture of the membranes, followed by delivery within 1 to 2 hours, this is the procedure of choice. Where the presence of an uneffaced, undilated cervix precludes early vaginal delivery, hysterotomy or cesarean section appears to be the optimum treatment. In cases with partial separation where the fetal heartbeat is present, and the cervix unamenable for vaginal delivery, speedy laparotrachelotomy should be performed.

Pre-eclampsia.—Eight sections have been performed for pre-eclampsia and, as noted in Fig. 2, all of these occurred during the last 3 years of the decade.

Patients exhibiting signs and symptoms of severe pre-eclampsia are hospitalized and vigorous desalting therapy together with reduction of the blood pressure is attempted. Electrolyte and fluid balance is corrected and urinary output is stimulated. Following 48 to 72 hours of treatment, with failure to control completely the pre-eclamptic process, if the cervix is found unready for vaginal delivery, a cesarean section is performed. If the pre-eclampsia is readily controlled the induction of labor need not be hurried. The exact week at which this pregnancy should be interrupted is still undecided.

In this clinic prior to 1948 severe pre-eclamptic cases, if controlled, were carried to 36 weeks or later before attempted induction. During one 4 month period 3 consecutive intrauterine deaths occurred in this type of patient at thirty-five weeks. Interruption is now carried out some time between the thirty-second and the thirty-fourth week and it is felt that with better pediatric care the 1,000 to 1,500 gram baby will have a better chance for survival ex utero after this period.

In the 8 pre-eclamptic patients whose pregnancies were interrupted by section, all infants survived.

Uterine Inertia.—This is a new indication for the use of cesarean section in this clinic. During the past 2 years 5 patients with primary inertia and 4 patients with secondary inertia have been delivered by laparotrachelotomy. All infants in this group survived. The presence of uterine inertia per se does not warrant the abdominal approach, but it seems to be indicated when inertia is superimposed upon relative degrees of disproportion, malpresentation, or fetal distress.

Type of Section

Fig. 3 shows the relative number of the various types of sections during the period of study. There were 125 low flap sections and 100 classical. A steady increase in the number of low flap from 6 in 1940 to 29 in 1949 may be noted.
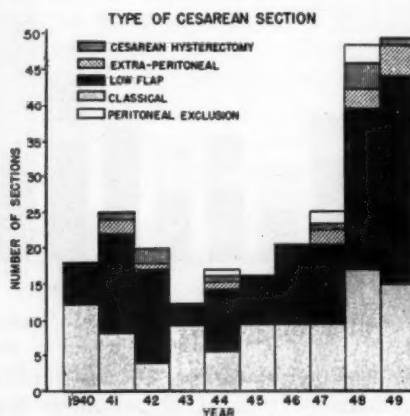
Fig. 3.—Type of cesarean section, 1940-1949.

The high number of classical sections still performed each year is the result of their use in cases of placenta previa and abruptio placentae. The wisdom of this selection is questionable, especially if vaginal delivery is to be attempted in subsequent pregnancies. Heffernan[8] concluded, after reviewing 14,776 low segment operations and 15,030 classical procedures, that laparotrachelotomy is over twice as safe as the classical section and has fewer subsequent complications. The policy now used in this clinic is to do a low flap section whenever possible, reserving the classical type for clean cases, where extreme haste is necessary to save maternal or fetal life.

Only 12 extraperitoneal and 4 peritoneal exclusion procedures have been performed during the period analyzed and these were done chiefly for teaching purposes. Where gross intrauterine infection exists and the patient is a primigravida or in the young age group, it is felt that extraperitoneal section offers the best prognosis. McCall[9] has reported 91 such cases of profoundly infected patients in whom the extraperitoneal approach was carried out with no maternal mortality and a fetal mortality of 8.8 per cent.

Cesarean hysterectomy was performed only 10 times, 6 times for leiomyomas, 3 for atonic uteri following abruptio placentae, and once for a grossly infected uterus in an elderly multipara. It is believed that cesarean hysterectomy in foully infected patients is dangerous, since it is a shocking procedure in a seriously ill patient and does not guarantee against peritoneal spill nor lateral extension through vessels and lymphatics. The sacrifice of the uterus in the primipara seems radical and needless if another procedure without higher maternal mortality is available. Therefore, only diseased or physiologically imperfect uteri are amputated at the time of section unless other extenuating circumstances exist.

Anesthesia

There has been a marked trend during the space of this decade from general to regional anesthesia for cesarean section. Table III shows that 119 sections (48 per cent) were performed with regional anesthesia—the majority of these being spinal. General anesthesia, chiefly gas-oxygen-ether or drop ether, was utilized up until 1943-1944. One maternal death from atelectasis occurred during this era. Subarachnoid block was then initiated, by means of Pontocaine in what is now considered excessive dosage, resulting in a second maternal death. Later 1 per cent procaine in dosages of 125-150 mg. with glucose, or given continuously per catheter was instituted. A third death occurred with this method. In 1948 a revision of policy occurred with the result that, at present, almost all sections are performed under 5 mg. of Pontocaine-glucose-ephedrine mixture or with a continuous spinal utilizing a minimal dosage of 1 per cent procaine. In cases of hemorrhage with actual or incipient shock, cyclopropane is used.

TABLE III. TYPE OF ANESTHESIA

1. Spinal		114
Pontocaine	56	
Procaine	46	
Continuous	12	
2. Gas-oxygen-ether		71
3. Cyclopropane		40
4. Drop ether		21
5. Local infiltration		4
6. Caudal		1

The importance of anesthesia in cesarean section is fully realized in this institution since all 3 maternal deaths in this report were directly attributable to the anesthesia. Since Lull[10] recently reported 1,000 consecutive cesarean sections performed under continuous spinal without a maternal death, it seems evident that our misuse rather than use of a particular method has been at fault. The several advantages offered by spinal anesthesia preclude reversion to previous methods.

The safety, controllability, and ease of administration of continuous spinal would seem to make it the ideal. Lull[10] has advised, however, that only an anesthetist trained in all forms of conduction anesthesia should supervise the procedure. In this hospital anesthesia is administered by graduate nurse student anesthetists and because of the simplicity of the single-shot, low-dosage Pontocaine, this method is presently in use.

Maternal Morbidity

The total number of patients classified as morbid was 109 or 43.3 per cent (morbidity defined as temperature rise to 100.4° F. or more some time during

two 24 hour periods excluding the first 24 hours). Fig. 4 reveals the steady
yearly decrease in morbidity from a high of 67 per cent in 1943 to 30 per cent
in 1949.

Table IV outlines the major postoperative complications.

TABLE IV.   COMPLICATIONS

A. *Infections.—*	
a. Wound breakdown	7
b. Pyelitis	1
c. Broad ligament abscess	1
B. *Pulmonary.—*	
a. Pulmonary infarction	3
b. Atelectasis	3
c. Pneumonia	3
C. *Hemorrhage.—*	
a. Postoperative hemorrhage	1
b. Postoperative shock	1
D. *Thrombosis.—*	
a. Phlebothrombosis	2
b. Thrombophlebitis	2
E. *Miscellaneous.—*	
a. Postoperative hernia	1
b. Postpartum psychosis	1
c. Hemolytic anemia	1
d. Aplastic anemia	1
e. Pernicious anemia	1

Fetal Mortality

The fetal mortality rate is shown in Table V. The gross rate for the 10
year period is 5.1 per cent (13 deaths). This is less than that reported by
Irving,[11] 6.8 per cent, Manahan and associates[12] 6.9 per cent, De Normandie[13]
8.2 per cent, and Dieckmann[14] 5.9 per cent. The over-all gross mortality rate
for all deliveries during the same period was 7.6 per cent. Correcting for in-
fants less than 1,500 grams, absence of fetal heartbeat on admission, and con-
genital abnormalities incompatible with life, the section fetal mortality rate is
2.3 per cent. Dieckmann[14] has stated that the fetal mortality ascribable to the
operation itself is less than 1.0 per cent.

TABLE V.   FETAL MORTALITY RATE

Over-all fetal mortality rate (gross)	7.6%
Cesarean fetal mortality rate (gross)	5.1%
Over-all fetal mortality rate (corrected)	2.7%
Cesarean fetal mortality rate (corrected)	2.3%

Table VI lists the gross fetal mortality rates in 8 cesarean section studies,
the average being 7.5 per cent as compared with 5.1 per cent reported in this
study.

Considerable controversy has existed concerning the relative fetal mortality
rates in operative vaginal delivery and cesarean section. Fig. 5 graphically
depicts the corrected* fetal mortality rate in high and midforceps in this clinic
as compared with that of cesarean section. It is evident that it has been much

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*Corrected for infants under 1,500 grams, absence of fetal heartbeat on admission, and
congenital abnormalities incompatible with life.

safer for the infant to have been delivered abdominally than by difficult operative forceps. The corrected rate for the entire period for high and midforceps is 6.6 per cent as compared with 2.3 per cent for section (Fig. 8). During this same period the incidence of high and midforceps was 1.4 per cent as compared with 1.0 per cent for cesarean section.

TABLE VI. COMPARATIVE FETAL MORTALITY RATES

YEAR	AUTHOR	HOSPITAL	GROSS FETAL MORTALITY RATE %
1934-1943	Irving[11]	Boston Lying-in	6.8
1922-1941	Manahan[12]	Johns Hopkins	6.9
1937-1941	DeNormandie[13]	State of Massachusetts	8.2
1942-1949	Dieckmann[14]	Chicago Lying-in	5.9*
1927-1936	King[15]	City of New Orleans	10.8
1942-1947	D'Esopo[1]	Sloane Hospital	3.7
1938-1947	Geiger[16]	Loyola University	7.8
1932-1946	Hennessy[2]	St. Vincents Hospital	9.7
		Average	7.5
1940-1949	Kistner	Cincinnati General	5.1

*Includes only infants weighing over 1,000 grams.

Fig. 6 shows the relationship of the increasing incidence of section plotted with the incidence of high and midforceps on the service fetal mortality rate. A steady decrease in the latter has occurred from a corrected rate in 1944 of 3.8 per cent to 2.2 per cent in 1949. The increased rate of high and midforceps in 1949 was due to a change in terminology classifying all rotations of the vertex as midforceps regardless of their station below the spines.
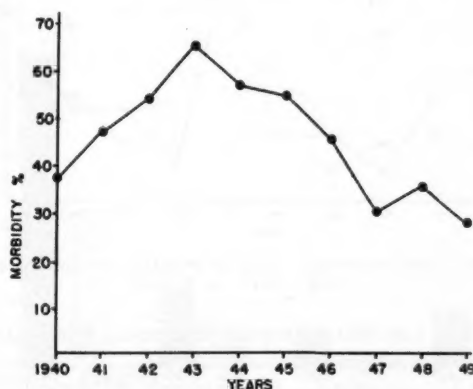
Fig. 4.—Morbidity percentage, 1940-1949.

Fig. 7 shows the relationship of the service corrected fetal mortality rate to the increased incidence of section and decreased incidence of the hydrostatic bag. There is almost a direct parallelism between diminishing fetal mortality rate and the decreased use of the bag.

Fig. 8 shows the comparative gross and corrected fetal mortality rates in the hydrostatic bag, high and midforceps, and cesarean section together with that for all deliveries.

Maternal Mortality

The total maternal mortality for the 10 year period was 1.1 per cent. All 3 deaths were directly attributable to the anesthetic and have been voted in

maternal mortality conferences as being "preventable" deaths. The last 2
were obviously due to inept use of spinal anesthesia.

The 10 year rate of 1.1 per cent is comparable with that reported by
Irving[11] of 1.3 per cent but it should be noted that the latter survey was of an
entirely different period, i.e., 1934-1943. The rate in this clinic is much higher
than that reported by Dieckmann[14] of 0.42 per cent for an 18 year period from
1931 to 1949. Improvement has occurred, however, during the past 5 years
with an increase in incidence and a decrease in mortality. Further reduction
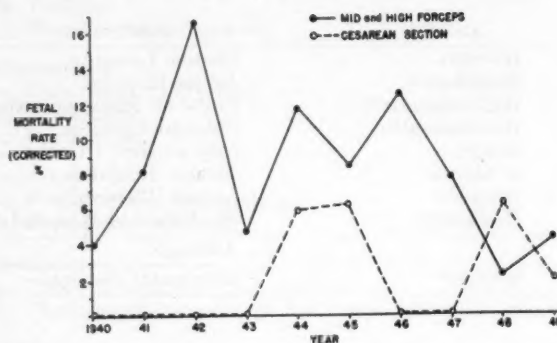
Fig. 5.—Corrected fetal mortality rate (per cent) in high and midforceps versus cesarean
section.
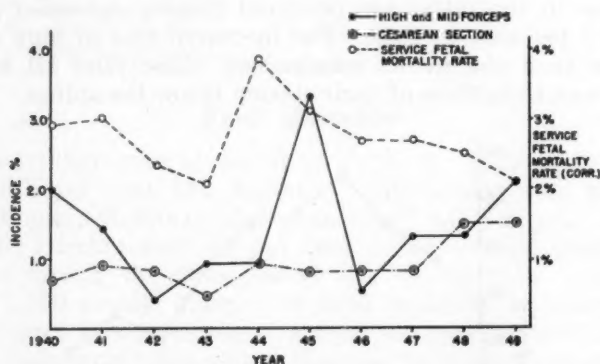
Fig. 6.—Corrected over-all fetal mortality rate in relation to incidence of high and midforceps
and cesarean section.

TABLE VII.   CESAREAN SECTION MATERNAL MORTALITY RATES

	NUMBER	INCIDENCE %	MORTALITY %
Boston Lying-in (1941-1945)	522	3.5	.57
Chicago Lying-In (1941-1945)	616	4.3	.32
Cleveland Maternity (1941-1945)	1,128	5.5	.62
Duke University (1941-1945)	105	1.8	.95
Johns Hopkins (1941-1945)	455	4.8	.21
Margaret Hague (1941-1945)	902	2.6	.66
New York Lying-In (1941-1945)	535	3.2	.37
Pennsylvania University (1941-1945)	840	7.0	.35
Stanford University (1941-1945)	429	6.2	0.00
Washington University (1941-1945)	227	1.6	0.00
Philadelphia Lying-in (1941-1948)	1,378	7.2	.07
Summary:	7,137	4.3	.37
Cincinnati—Bethesda (1935-1945)	205	1.3	2.9
Cincinnati—General (1941-1945)	90	0.7	2.2
Cincinnati—General (1940-1949)	251	1.0	1.1

is necessary in this respect since it has been suggested that the maternal mortality rate in cesarean section should not exceed 0.1 per cent. Several clinics have approached or bettered this rate. Dieckmann[14] has reported over 1,100 consecutive sections without a death and Lull and Ullery[10] describe 1,628 sections with only one death, that one being due to leucemia.

Table VII outlines the section maternal mortality rates of 11 leading teaching clinics together with the incidence of the operation. In 7,137 procedures, where the incidence was 4.3 per cent, the maternal mortality rate was 0.37 per cent. In both Cincinnati hospitals tabulated, however, showing a much diminished incidence, the maternal mortality rate was 6 to 7 times as great.
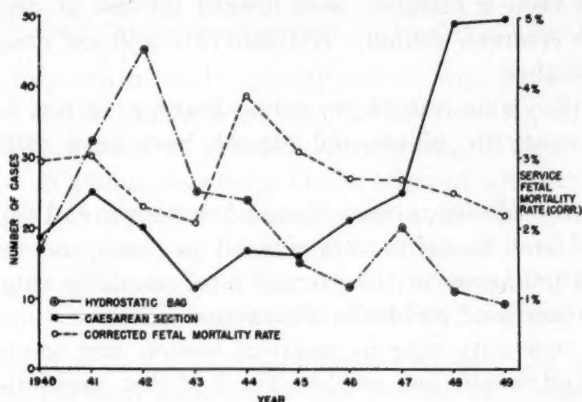
Fig. 7.—Corrected over-all fetal mortality rate in relation to incidence of hydrostatic bag and cesarean section.
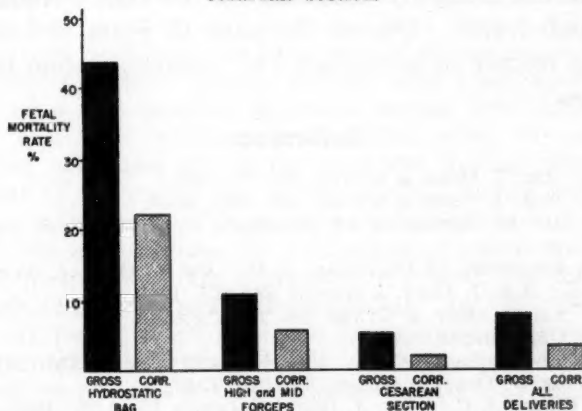
Fig. 8.—Gross and corrected fetal mortality rates.

During this 10 year period of analysis the maternal mortality rate in operative vaginal delivery was 1.0 per cent. It is apparent that it has not been more hazardous to deliver a patient abdominally than by the operative vaginal approach.

Summary and Conclusions

1. A survey of 251 cesarean sections occurring during the interval 1940-1949 is presented.

2. A doubling of incidence has occurred during the last 2 years of the period but the over-all incidence of 1 per cent remains low as compared with

that of other teaching clinics. The incidence was twice as high in the Negro race as in the white.

3. The chief indications were cephalopelvic disproportion, repeat sections, and hemorrhage. New indications during the last 2 years have been pre-eclampsia and uterine inertia.

4. An increasing number of the laparotrachelotomy type section is being performed both in clean and potentially infected cases. The classical section should be relegated to the clean case in which fetal or maternal life depends upon haste.

5. There has been a marked trend toward the use of regional anesthesia, chiefly spinal, for cesarean section. Extreme care and low dosage are necessary adjuncts to this method.

6. The morbidity rate was 43 per cent. During the last 5 years penicillin, sulfonamides, aureomycin, blood, and oxygen have been utilized to diminish the morbidity.

7. The chief complications were wound breakdown and pulmonary disease.

8. The gross fetal mortality rate was 5.1 per cent and the corrected rate 2.3 per cent. A diminution in the over-all fetal mortality rate has been shown to accompany the increased incidence of cesarean section.

9. The fetal mortality rate in cesarean section was one-tenth of that obtained with the hydrostatic bag and one-third of that associated with high and midforceps during the same period.

10. The maternal mortality rate was 1.1 per cent. Anesthesia accounted for all 3 maternal deaths. During the past 10 years it has not been more hazardous for the mother to be delivered by cesarean section than by operative vaginal procedures.

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PREGNANCY IN IDIOPATHIC ULCERATIVE COLITIS

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ONE is frequently consulted by young women who have suffered from an idiopathic ulcerative colitis regarding the advisability of having children. The decision reached is based on the clinical judgment of their individual medical status, and not on actual knowledge of the effect of pregnancy on the course of this disease. When pregnancy is considered inadvisable, and the advice has been followed, there is no way to determine what would have been the outcome had the pregnancy been attempted. The frustration resulting from such advice has never been determined, nor its possible effect upon the course of the disease.

The paucity of data on this problem implies that very few, if any, physicians have had sufficient personal experience with it. In 1931, Barnes and Hayes[1] reported three fatal cases; two of these patients developed a colitis in the puerperium and rapidly succumbed to the disease, while one had an antecedent colitis, aborted at four months, and died five days later. All had toxemia of pregnancy. Autopsies confirmed the diagnosis of ulcerative colitis in two, and ulcerative enterocolitis in one. Baum[2] in the same year reported a case with autopsy findings of a five months pregnant woman who developed an acute ulcerative colitis and died within thirteen days after the onset. In 1936, Saegesser[3] reported two cases of ulcerative colitis during pregnancy. In the first case, the onset of the colitis was in the seventh month and became aggravated during the puerperium. The patient gradually improved under medical management. In the second case, the first signs of colitis were recognized in the fifth month of pregnancy. The symptoms increased, but following a normal delivery of a viable child they gradually subsided. In 1938, Buzzard and associates[4] described six patients, all of whom experienced relapses of their colitis during pregnancy and childbirth. In the same year, Feder[5] mentioned five patients with acute recurrences during pregnancy. In 1939, Bargen, Nunez, and Mussey[6] reported seventeen cases of ulcerative colitis with eighteen deliveries and four miscarriages. After nine of the deliveries, the symptoms were improved, and in five patients they became aggravated. There was no change in symptoms in three patients; thus they reported 29 per cent aggravated, 53 per cent improved, and 18 per cent unchanged. In a group of patients who miscarried, three were improved after the miscarriage, and one remained unchanged. The authors suggest that the variability of the reaction of ulcerative colitis in pregnancy is dependent upon protein metabolism present, with the suggestion that in those cases where the protein requirement is met, the cases become mild, and in those where the ulcerative colitis is attendant upon an overwhelming infection, the symptoms become worse after pregnancy. In 1948, Kirsner and co-workers[7] reported nine exacerbations of an ulcerative colitis accompanying pregnancy, while in seven cases the pregnancy was uneventful.

The largest series yet reported of patients with ulcerative colitis associated with pregnancy is that of Felson and Wolarsky,[8] in 1948, in which 34 women had 50 gestations. In 26 patients, chronic ulcerative colitis antedated the onset of pregnancy for periods ranging from three to seven years. In 8 patients, the symptoms of ulcerative colitis developed during pregnancy. It is assumed from their report that these 8 patients also had antecedent ulcerative colitis, and not the acute phase of the disease, but merely a re-exacerbation of symptoms. The writers found that in 58 per cent of the pregnancies the ulcerative colitis improved, in 12 per cent it was unchanged, and in 30 per cent symptoms of ulcerative colitis were aggravated.

In the study of this problem, a pooling of our private cases and all the cases on record in the Boston City and Boston Lying-in Hospitals was made.*

Material

Thirty-three cases of idiopathic ulcerative colitis were collected. There were 46 gestations. Our patients are divided into four groups: Group I consists of patients with an antecedent ulcerative colitis quiescent at the onset of pregnancy; Group II, of patients in whom the antecedent ulcerative colitis was in an active stage at the onset of pregnancy; Group III, of patients in whom the ulcerative colitis developed during pregnancy; and Group IV, patients in whom the ulcerative colitis developed in the puerperium.

As shown in Table I, Group I included twenty pregnancies. In these patients, the disease was chronic, and in most of them several acute exacerbations had been observed. One patient conceived three times, having had two full-term pregnancies followed by one spontaneous miscarriage.

Another patient deserves special mention in that she had the only cesarean section in the entire group. She had ulcerative colitis for over three years. At the time she conceived, the disease had been quiescent for one and one-half years. During the first six and one-half months of her pregnancy, the colitis remained controlled by diet, rest, and medication. Then, without a demonstrable cause, the disease became reactivated. She developed a high septic temperature, had uncontrollable diarrhea, and severe crampy pain. She rapidly became dehydrated and developed a severe hypochromic anemia and slight pitting edema of the ankles. Because of her poor condition, cesarean section was done at 7½ months, and a viable child delivered. The patient had a stormy convalescence, but recovered within 12 weeks and remained essentially symptom free for over four years.

The one therapeutic abortion in this group was done because of a psychoneurosis.

TABLE I. GROUP I. 20 CASES OF ULCERATIVE COLITIS QUIESCENT SIX MONTHS TO EIGHT YEARS PRIOR TO ONSET OF PREGNANCY

EXACERBATION		NO EXACERBATION	
During pregnancy	5	Pelvic deliveries	11
Post partum	2	Therapeutic abortion (psychosis)	1
		Spontaneous miscarriage	1
Total	7 35%	Total	13 65%

Table II concerns our Group II of 17 pregnancies. Diarrhea was the predominant symptom in these patients. The stools contained either mucus, pus, or blood. Some patients had anemia and slightly elevated temperatures. There were five therapeutic abortions, one patient having had two. All of these did

well postoperatively, and their reactivated colitis subsided rapidly under medical treatment. The follow-up observations of these four patients for periods ranging from one to six years revealed no exacerbations in their disease which could be attributed to the operative intervention.

TABLE II.   GROUP II.   17 CASES OF ULCERATIVE COLITIS ACTIVE AT ONSET OF PREGNANCY

SYMPTOMS AGGRAVATED	
During pregnancy	16
Post partum	1
Total	17 100%
Pelvic deliveries	12
Therapeutic abortion	5

A composite picture of Groups I and II is shown in Table III. Two patients had three conceptions each. One had one full-term delivery followed by a spontaneous miscarriage. Nine women conceived twice each, and all had full-term deliveries. Thirteen women conceived once each, and, of these, eight had pelvic deliveries at term. The symptoms subsided fairly soon postpartum in 14 cases, and continued unabated in 4, terminating fatally in 2, eight and twenty months later, respectively. In the former, an ileostomy was performed eight months after delivery and resulted in the death of the patient, six days later. In the second fatal case, ileostomy was repeatedly urged upon the patient, but persistently refused.

TABLE III. 24 PATIENTS, 37 GESTATIONS

Pelvic deliveries	29
Cesarean sections	1
Spontaneous miscarriages	1
Therapeutic abortions (one for psychoneurosis)	6
No exacerbation of symptoms	15
Exacerbation or increase in symptoms	24
Onset of Symptoms in 24 Gestations.—	
1st trimester	11
2nd trimester	4
3rd trimester	6
Post partum	3

Group III concerns five patients, as noted in Table IV.

The first patient was a 35-year-old para ix with six living children and with no previous history of ulcerative colitis. She developed symptoms of diarrhea at two months of pregnancy, and despite diet and the usual medical regime, she gradually became worse. Sigmoidoscopy and barium enema two months after onset revealed extensive involvement of the large bowel. The following month she became extremely ill and there was evidence of a toxic hepatitis. At seven months of pregnancy and five months after the onset of the illness, because of marked distention, an ileostomy was done as an emergency procedure. Shortly afterward she delivered spontaneously a stillborn female infant, and several days later she died. Autopsy revealed extensive disease with localized perforations of the large bowel and the jejunum, a subacute hepatitis, and multiple small pulmonary emboli.

The second patient was a 34-year-old para ii with no previous history of ulcerative colitis, who developed symptoms of diarrhea and acute left lower back pain at about four months of pregnancy, followed by the occurrence of pain in the right flank and right costovertebral region, and a fever of 102° F. The urine culture showed B. coli, and the diagnosis of pyelitis was made. Although the pyelitis improved on the third day after treatment with sulfadiazene had been instituted, the temperature rose to 104° F. with persistence of the diarrhea. The patient had 12 stools a day. Agglutination tests for typhoid, paratyphoid,

and brucellosis were all negative on repeated tests. A severe secondary anemia developed, with a red blood count of 2.6 million and a hematocrit of 29 per cent. She had been treated with Crysticillin prior to admission to the hospital. This was discontinued and aureomycin begun, but after several days the aureomycin was discontinued and penicillin therapy reinstituted along with intravenous sulfadiazene. She was given five blood transfusions of 500 c.c. each. One week following admission, it was noted that the right lobe of the liver was enlarged, and the diagnosis of a liver abscess was entertained. However, the fever subsided gradually following this but the symptoms of diarrhea recurred. She rapidly went downhill and four weeks later she had a spontaneous miscarriage of a one-pound infant, and she died 24 hours after delivery. The post-mortem showed acute ulcerative colitis and acute peritonitis.

The third patient was admitted to the hospital for diarrhea and lower abdominal crampy pain of eight weeks' duration. Four days later she had a spontaneous miscarriage, followed by a severe exacerbation of the intestinal symptoms. Within 11 days she died as a result of an acute perforation of the sigmoid and a spreading peritonitis. These findings were confirmed by autopsy.

The fourth patient had very acute symptoms during the last six weeks of pregnancy and the ensuing sixteen months. This was followed by a remission lasting eighteen months, and then she became pregnant again. So far she has remained asymptomatic.

The fifth patient died two days after a normal spontaneous delivery, and 12 days after the onset of symptoms. An autopsy showed an acute and chronic ulcerative colitis involving the entire colon, but more marked in the ascending and proximal portions of the transverse colon.

TABLE IV. GROUP III. ACUTE ONSET OF ULCERATIVE COLITIS DURING PREGNANCY

ONSET	TYPE OF DELIVERY	RESULT	AUTOPSY
2 months	Spontaneous	Died 5 months after onset following ileostomy	Acute ulcerative colitis Ileostomy Perforated jejunum Subacute hepatitis
4 months	Spontaneous miscarriage	Died 10½ weeks after onset, 24 hours post partum.	Acute ulcerative colitis Acute peritonitis
4½ months	Spontaneous miscarriage	Died 11 days puerperium	General peritonitis Perforation of bowel
7½ months	Normal delivery	Stormy 16 months Remission 18 months. Now pregnant again.	
38½ weeks	Normal delivery	Died 12 days post partum	Pulmonary edema Bronchopneumonia Acute chronic ulcerative colitis.

Group IV includes four patients who developed an acute ulcerative colitis after normal pregnancy and delivery.

One patient, ten days post partum, developed fever, profound secondary anemia, distention of the abdomen, and diarrhea. A question of septicemia or pelvic peritonitis was raised. She continued a downhill course with uncontrollable diarrhea and a picket-fence temperature for the next 33 days, when she died. The autopsy revealed the entire colon to be involved in a severe ulcerative colitis.

Another patient developed a severe diarrhea immediately after her third child was delivered. She had no previous intestinal disturbances. During the puerperium she had ten to twelve watery bowel movements a day. There was no fever. The number of stools gradually subsided, but the consistency remained watery to pasty. Despite adequate medical treatment, she lost weight and strength and became anemic. Sigmoidoscopy revealed the rectal mucosa to be inflamed and swollen. It bled on the slightest touch. Scattered throughout the rectum and visible portion of the sigmoid were numerous pinpoint ulcerations. This patient was observed for 17 months, during which time her symptoms gradually subsided, but the mucosa of the rectum and sigmoid did not become normal.

A third patient developed a purulent rectal discharge and diarrhea on leaving the hospital after a normal delivery. The stools were loose, watery, and contained traces of fresh red blood. These symptoms persisted, and eleven months later she was readmitted to the hospital; at that time she showed evidence of recent weight loss, dehydration, and hypochromic anemia. There was no elevation of the temperature. The abdomen was distended and tender in the suprapubic region. Sigmoidoscopy revealed an active ulcerative colitis. A barium enema showed the entire colon to be involved. She continued on a rapidly downhill course. A transverse ileostomy was performed on the fourteenth hospital day. She died 10 days later. An autopsy permit was denied.

The fourth patient developed chills and fever three weeks after the birth of her third child. One week later bloody diarrhea was noticed. The diarrhea rapidly became worse, and on admission to the hospital ten days later, she had 20 to 30 bowel movements a day. Her fever persisted and was irregular. She rapidly became anemic and dehydrated. Sigmoidoscopy revealed many ulcerations throughout the visible mucosa, which was inflamed and oozed readily. Barium enema disclosed an ulcerative colitis involving the entire colon. Because the patient did not respond to medical treatment, a transverse ileostomy was performed on the thirty-second hospital day. She died five days later. An autopsy permit was refused.

TABLE V. GROUP IV. ACUTE ONSET OF ULCERATIVE COLITIS IN PUERPERIUM

ONSET	TYPE OF DELIVERY	RESULT	AUTOPSY
10 days post partum	Normal pelvic	Died 33 days after onset	Severe ulcerative colitis
1 day post partum	Normal pelvic	Symptoms subsided during next 17 months	
10 days post partum	Normal pelvic	Symptoms 11 months, then transverse ileosteomy. Died 10 days postoperatively	Autopsy denied
3 weeks post partum	Normal pelvic	Transverse ileostomy 4½ weeks after symptoms. Died 5 days postoperatively	Autopsy denied
		Mortality 75%	

In the entire group, therefore, there were 36 babies delivered. In none of these cases were there any serious obstetrical complications. One stillbirth occurred. No case of pre-eclampsia or eclampsia was encountered. The symptoms and signs which indicated increased activity of the ulcerative colitis, during pregnancy or in the puerperium, were local, general, or both. The local symptoms were increased diarrhea, the stools containing mucus, pus, and blood. Crampy pain or abdominal distress, excessive flatus, and rectal tenesmus either recurred or became aggravated. The general symptoms were fever, anorexia, anemia, hypoproteinemia, loss of weight, weakness, and in some patients, toxic arthritis and pyoderma. In no case could an improvement in the ulcerative colitis be established as a result of a pregnancy or pregnancies. As far as could be determined, the extent of the involvement of the colon played no part in the reactivation of the process, and in those cases in which a recent study of the colon permitted a definite statement as to the amount of colon involved before a pregnancy, no regression of the ulcerative colitis occurred during a pregnancy or immediately post partum. To the contrary, in 13 cases, extension of the process could be demonstrated by sigmoidoscopy and barium enema after delivery, irrespective of the symptoms. No extension of the process or aggravation of symptoms was found by direct examination in the six cases of therapeutic abortions.

Two patients deserve special mention. Both had ileostomies for heretofore intractable ulcerative colitis. One had had the operation three years before conception, had an uneventful pregnancy and delivery, and an uneventful follow-up for two years afterward. The other

patient conceived four months after her ileostomy operation. She, too, had an uneventful pregnancy, and was delivered by a low forceps operation. Her puerperium was normal. However, her further course is unknown to us.

Diagnosis

The diagnosis of ulcerative colitis is made first with appearance of its usual symptoms, namely, frequent stools, usually soft or watery, with or without blood, mucus, and pus. In the more acute cases or in acute exacerbations of chronic cases, there is likely to be an irregular, more or less persistent febrile course, loss of weight, emaciation, dehydration, and anemia. The diagnosis is confirmed by sigmoidoscopic examination in which inflammatory changes in the mucosa of the rectum and colon are shown, frequently with acute or chronic ulcerations, or simply an oozing mucous surface demonstrated by gently wiping the mucosa. Sigmoidoscopy, properly conducted, is a safe procedure in all stages of pregnancy. The same applies to the barium enema procedure, provided no unusual pressure is exerted by the roentgenologist. Small mucosa abscesses may be demonstrated. The extent of involvement is determined by barium enema. It is our belief that sigmoidoscopy in competent hands is not contraindicated in the presence of pregnancy. It is true that sigmoidoscopic examination is more difficult in the presence of an advanced pregnancy; however, important information can be obtained and the examination can be done without any danger to the patient. Other types of colitis must be excluded, namely, amebic infection, bacillary dysentery, lymphogranuloma inguinale, and other specific forms. They can be excluded by stool examinations, agglutination tests, and blood culture.

Treatment

The treatment of the cases discussed here was carried out somewhat differently in private practice and in the two hospitals. During the first trimester of pregnancy, if a patient did not rapidly respond to rest, symptomatic treatment, and an attempt at specific medication, an abortion was advised, and, in every instance in this series, accepted by the patient. There were five such cases, and the results were very gratifying in that the symptoms subsided rapidly.

If the patient was first observed and the diagnosis of ulcerative colitis made in the second or third trimesters of pregnancy, every attempt was made to guide the patient through the pregnancy. In only one instance was a premature delivery considered advisable. This patient was delivered by cesarean section without aggravation of the colitis.

The medical management consisted of either relative or absolute rest, dependent upon the severity of the exacerbation and the presence or absence of an elevated temperature and pulse rate. The patients were given a high caloric, high protein, and low residue diet. Supplementary vitamins were given in large dosage by mouth, as a rule, but parentally in a few instances. Parenteral liver extract was used in most cases. Proper hydration of the patient was insisted upon. In view of the increased need for calcium in pregnancy, and because some patients could not partake of milk without aggravation of symptoms, supplementary calcium was routinely given. When an anemia was present, iron in adequate doses was prescribed, and the response to this medication carefully observed by frequent observations of the cellular elements of the blood. Blood transfusions were resorted to in the cases which did not respond to iron therapy. Plasma transfusions were given in cases of hypoproteinemia regardless of a reversed albumin globulin ratio. Other drugs were employed as indicated. Belladonna, atropine, or their substitutes, sedatives, bismuth, kaolin, and pectin were used in many cases with variable effect. Opium and its various derivative

were largely abstained from because of their transmission through the placentas to the fetuses. In the more recent cases, Demerol was administered when indicated.

Sulfonamides of the absorbable and nonabsorbable type were used in most of the more recent cases in an attempt to influence the intestinal flora. In six cases penicillin, in three cases streptomycin, and in one case aureomycin was given. None of the antibiotics appeared to influence the course of the ulcerative colitis. Although in none of the patients were *Endamoeba histolytica* demonstrated, emetine was used in a therapeutic trial in three cases without a demonstrable effect. Psychogenic factors were likewise considered, and an attempt at psychotherapy was made, but no formal psychoanalytic measurements were undertaken in these cases. The quiescent cases of ulcerative colitis in pregnancy were generally managed in a similar way, though in many patients no medicinal measures were necessary. However, careful diet, relative rest, and supplementary vitamins and calcium were insisted upon routinely. Ileostomy was resorted to during pregnancy in one patient and resulted in a fatality. In two patients ileostomy was done prior to the pregnancy, and in three patients, the operation was performed after delivery. In one case, though ileostomy was advised, it was refused by the patient.

Comment

As stated above, this study was undertaken in an attempt to determine what effect pregnancy has on the course of idiopathic ulcerative colitis. In the summation of statistics in Table III, comprising Groups I and II, it is to be noted that reactivation of the dormant colitis, or an aggravation of a previously active one, was observed in 24 pregnancies out of 37 studied. In the remaining 13 instances, no noticeable effect on the ulcerative colitis, quiescent or active, could be demonstrated, either symptomatically or by direct examination. In no case where the patient's condition improved could such improvement be attributed to the pregnancy. The morbidity caused by the exacerbation of the disease varied from case to case, and in retrospect it is difficult to evaluate except in instances where a quiescent disease became reactivated, or where a marked aggravation of symptoms and signs occurred. Because of these considerations only striking changes were considered, and minor or fleeting exacerbations were not included.

One should always bear in mind that the course of an idiopathic ulcerative colitis is unpredictable at all times, and exacerbations of the disease occur spontaneously. Nevertheless, the high percentage of increased morbidity from ulcerative colitis during pregnancy, namely 35 per cent in Group I, and 100 per cent in Group II, is and should be considered before conception is contemplated, and before it is decided whether pregnancy should be allowed to continue on when complicated early by severe activation of the disease. The 35 per cent aggravation of a quiescent ulcerative colitis during pregnancy and the puerperium is distinctly higher than could be expected in this disease not complicated by a pregnancy. The seriousness of this complication of pregnancy is even more emphasized in Groups II and III. In Group II, where pregnancy started in the presence of an active ulcerative colitis, 100 per cent showed exacerbations, or aggravation of symptoms. There was no immediate mortality in Groups I and II, though in Group II there were two deaths, 8 and 20 months after delivery, representing an ultimate mortality of 5.5 per cent. In Group III, where we encountered the fulminating type of acute ulcerative colitis, the morbidity was severe and the mortality was very high, namely, 80 per cent. Thus one must conclude that pregnancy complicated by acute idiopathic ulcerative colitis is likely to have a high mortality. Though there were only 5 therapeutic abortions

out of 17 conceptions in Group II, there was an ultimate mortality of 5.5 per cent. This emphasizes the fact that patients who have an ulcerative colitis should avoid pregnancy while the disease is in an active stage, since the disease itself tends to produce inanition and generally decreased resistance. Should pregnancy occur and the patients be observed in the first trimester of pregnancy, then therapeutic abortion should be performed. If the ulcerative colitis be reactivated during the second and third trimesters of pregnancy, it would seem fair to continue on with the pregnancy, unless the intestinal symptoms should not be controllable by usual methods, in which case interruption of pregnancy would not be contraindicated. With the combined efforts of the obstetrician, gastroenterologist, and psychiatrist, many of these patients can be carried to term. Pelvic delivery is of course preferable to cesarean section. Because of intestinal contractions during and following spinal anesthesia, it is best to use general anesthesia for delivery.

In recent years attempts have been made to apply psychiatric treatment to many medical illnesses, especially those of unknown cause. Idiopathic ulcerative colitis is no exception; there have been several reports which impress one that this disorder has a psychogenic element. Detailed psychiatric studies in ulcerative colitis patients, conducted by V. P. Mahoney and his associates,[9] point to the complex neurotic traits commonly observed in neuroses and other psychosomatic conditions. It is of course obvious that these personality traits are not specific as regards the etiology of ulcerative colitis. However, it is no doubt true that an understanding of them in each patient may be useful in combined obstetrical and gastroenterological treatment. It is therefore felt that the understanding psychiatrist can add considerably to the armamentarium thus far used in the treatment of idiopathic ulcerative colitis.

Summary

Forty-six gestations in 33 patients with idiopathic ulcerative colitis are reported. They are classified in four groups: antecedent ulcerative colitis with a pregnancy occurring in the quiescent or in the active stage of the disease, respectively, and an acute ulcerative colitis developing during gestation or in the puerperium.

In Group I, 7 out of 20 patients (35 per cent) showed evidence of reactivation during pregnancy or in the puerperium but there were no deaths.

In Group II, all 17 cases (100 per cent) became aggravated during this period. Though there were no immediate deaths, 5.5 per cent of the patients eventually succumbed to the disease.

In Group III, 4 out of the 5 patients with an acute onset of ulcerative colitis during pregnancy died (a mortality of 80 per cent), irrespective of medical treatment or combined medical and surgical management.

In Group IV, 3 out of 4 patients who had an acute onset of ulcerative colitis in the puerperium died (75 per cent).

Therapeutic abortion is recommended in the severe cases of ulcerative colitis in the first trimester of pregnancy and careful medical management thereafter. It is recommended that the obstetrician, gastroenterologist, and psychiatrist work as a team in caring for the patient with idiopathic ulcerative colitis.

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127 BAY STATE ROAD

INTRATUBAL TERM PREGNANCY WITHOUT RUPTURE: REVIEW OF THE LITERATURE AND PRESENTATION OF DIAGNOSTIC CRITERIA

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ECTOPIC pregnancy, by definition, includes all cases of pregnancy outside the uterine cavity. The incidence of this complication has been estimated by Schumann[49] at 1 in 300 pregnancies. Mall[37] has further postulated that about 1 per cent of ectopic gestations go to term but clinical experience suggests that this figure is exaggerated. Intratubal pregnancy without rupture at or near term with a fully developed fetus is, therefore, an obstetrical rarity. A total listing of all the possible extrauterine positions where nidation and development might occur would include the sites listed in Table I. An especial attempt has been made to use precise terms in this table. The two varieties of term ectopic gestation most commonly discussed in the literature and in textbooks are (1) abdominal pregnancy of which some 258 cases have been reported[3] and (2) ovarian pregnancy of which some 100 cases have been reported but only a lesser number (approximately 60) have been authenticated.[11]

TABLE I. POSSIBLE SITES OF EXTRAUTERINE PREGNANCIES

Primary abdominal	Intraligamentous
Secondary abdominal	Tubouterine
Primary ovarian	Pregnancy in a rudimentary or accessory uterine horn
Ovario-abdominal	Pregnancy occuring after subtotal hysterectomy
Tuboovarian	In the cervical stump
Tuboabdominal	In a Fallopian tube
Intratubal	Cervical
Ampullary	
Isthmian	
Interstitial	

We recently encountered a case of intratubal pregnancy which went to term without rupture. We have reviewed the literature concerning this interesting obstetrical complication in considerable detail. It is our purpose (1) to establish criteria by which a true, unruptured intratubal pregnancy occurring at or near term may be recognized, (2) to consider, as briefly as possible, comments made in the literature, which have seemed of especial significance to us, (3) to list the cases previously reported in the tables, and (4) to present our case.

Critera for the Diagnosis of True Intratubal Pregnancy Near or at Term, Without Rupture of the Tube

We suggest that the following salient factors be established as necessary for the diagnosis: (1) that complete extirpation of the fetal sac and products of conception be achieved by salpingectomy; (2) that there be no gross or micro-

scopic evidence of tubal rupture; (3) that ciliated columnar epithelium be demonstrated at some few points in the inner lining of the sac, and (4) that smooth muscle be found in the sac wall at multiple sites and at considerable distances from normal, undilated tube.

Ideally, for the purpose of classification, cases of intratubal pregnancies at term without rupture would be isthmian in location with normal undilated tube both proximally and distally but it seems to us that if the aforementioned four criteria can be fulfilled the diagnosis is justified. The wisdom of using the term "true" intratubal pregnancy for those pregnancies in the isthmian portion of the tube and "pseudo" for those nearer the ampullary portion or in the ampulla was considered but seemed unnecessarily rigid in view of the rarity of this condition.

The fundamental concept in our minds is, therefore, that of a fetus and placenta enclosed within the Fallopian tube to such a degree that no other pelvic or intra-abdominal organ is involved in the formation of the sac and that salpingectomy alone is curative.

Comments From the Literature

Certain comments that have appeared in the literature seemed of importance to us. These are as follows:

Presence of Adhesions.—The attachment of the enlarged tube by adhesions was particularly emphasized by Brugeas,[6] Lazarevic,[31] and Miller.[39] Friction between the serosal surface of the enlarging tube and adjacent organs was postulated as a cause, and Miller[39] suggested that the adhesions might represent an attempt by nature to deliver additional blood to the structure.

Hysterosalpingography.—The technique of injecting a radiopaque substance into the uterus and tubes was rarely used. Ferrari, Houèl, and Jahier[16] employed it to advantage to obtain a correct preoperative diagnosis. This procedure should be more widely used in cases of suspected, advanced ectopic gestation in which there is no infection and fetal death has occurred.

Microscopy.—Microscopic examination of the fetal sac was not employed widely enough in the cases reported in the literature. As indicated in the preceding paragraphs, this procedure is necessary for precise diagnosis.

Placental Site.—The matter of placental location was particularly discussed by Schumann,[48] who postulated that the site of placentation might have some bearing on the degree of fetal development and the extent to which the tube might grow. He suggested that when the placenta is located on the inferior surface of the tube and is, therefore, in relatively close contact with the mesosalpinx the greater elasticity and vascularity of this area would permit greater tubal hypertrophy and consequently less danger of tubal perforation by the long villi.

Diagnosis at Necropsy.—In several cases, notably those of Varner and Green[56] and Williamson,[65] the diagnosis was confirmed at necropsy. Williamson[65] stated in his article that reports of only 9 cases were recorded in the literature up to 1928.

Pain During Pregnancy.—An uncomfortable pregnancy with some episodes of "threatened abortion" was mentioned in the majority of the cases. It would seem that the presence of severe pain might raise the issue of tubal rupture.

Surgical Procedures.—Several writers commented that during the early stage of the operative procedure employed for relief of this condition they believed themselves to be dealing with the uterus while they were actually handling the Fallopian tube. This is a misconception which we shared.

History.—Histories of false labor, unsuccessful attempts at induction, unexplained intrauterine fetal deaths, abnormal presentations, and absence of effacement and dilatation of the cervix were frequently noted.

TABLE II. FORTY-FOUR CASES OF INTRATUBAL PREGNANCY WHICH WENT TO TERM OR NEAR TERM WITHOUT RUPTURE

AUTHOR	DATE	AGE OF MOTHER IN YEARS	GRAVIDA	PARA	DURATION OF GESTATION IN MONTHS	LAPAROTOMY PERFORMED	SIDE	FATE OF CHILD	FATE OF MOTHER
Osgood[42]	1746			i	Term	16 years after term	Left	Death	Death
Brendel[5]	1883	32	ii	0	8	8 months after last menstrual period		Death	Recovery
Folet[19]	1895	36			Term	15 years after fetal death		Death	Recovery
Lejars[32]	1904	35	vi	ii	7	9 months after last menstrual period	Left	Death	Recovery
Grunbaum[23]	1909				Term			Death	Recovery
Morris[41]	1910				Term	13 months after last menstrual period	Right	Death	Recovery
Kleemann[28]	1912				Term	9½ months after last menstrual period	Left	Death	Death
Knaggs and Walker[29]	1912				Term	11 months after last menstrual period		Death	Recovery
Cheput and Marchal[8]	1913				Term	3 years after fetal death		Death	Recovery
Conway[10]	1913	23	iv	i	Term	2 months after term	Right	Death	Recovery
Schmit[47]	1913				Term			Survival	Recovery
Krasnopolski[30]	1913							Survival	Recovery
Werner[62]	1914	26		i	8	8 months after last menstrual period	Right	Death	Recovery
Westenmark[64]	1917	27	ii		8	8 months after last menstrual period	Right	Death	Recovery
Smith[52]	1920	32	iv	iii	9	9 months		Survival	Recovery
Lichtenstein[33]	1920	34	iii	ii	Term	15 months after last menstrual period		Death	Recovery
Lichtenstein[33]	1920	34	ii	i	Term	10 months after last menstrual period	Right	Survival	Recovery
Hisgen[24]	1921	27	ii	i	Term	6 weeks after fetal death	Right	Death	Recovery
Rosenblatt[45]	1923	36	ii		Term	13 months after last menstrual period	Left	Death	Recovery
Hoehne[25]	1923	30			7½	7½ months after last menstrual period	Right	Survival	Recovery

Hoehne[25]	1923	32	ii		36 weeks		Left	Death	Recovery
de Araujo[12]	1925	29	i	0	Term	Term	Right	Survival	Death
Kisman[27]	1927	25	i	0	Term		Left	Death	Recovery
Ferrari, Houel, and Jahier[16]	1927	35	iv	iii	Term	3 months after fetal death	Left	Death	Recovery
Williamson[65]	1928		iv	iii	Term	At term	Right	Survival	Death
Lazarević[31]	1929	36	i	0	7	7 months after last menstrual period	Left	Survival	Recovery
Brugeas[6]	1929			iv	Term	11 months after last menstrual period	Left	Death	Recovery
Watters[61]	1931	23	i	0	Term	11 years after term	Right	Death	Recovery
Tottenham[54]	1934	39	iii	ii	Term	6 weeks after fetal death	Right	Death	Recovery
Tottenham[54]	1934	23	i	0	7¼		Left	Death	Recovery
Fink[17]	1934	31			Term	2 years after fetal death	Right	Death	Recovery
Wlassow[66]	1936				Term			Death	Recovery
Schumann[48]	1936	22	i	0	Term	24 hours after fetal death	Left	Death	Recovery
Decanio[13]	1937	38		iii	Term	At term		Death	Recovery
Varner and Green[56]	1937	20	iii	ii	Term	Several weeks after term		Death	Death
Miller[39]	1938	23	ii	i	Term	2 months after term	Right	Death	Recovery
Christitch[9]	1939	30	iii	ii	Term	1 month after term	Left	Death	Recovery
Wanserley[59]	1940	19			Term	11 years after term	Right	Death	Recovery
Slinger[51]	1940	42		vi	Term	At term	Left	Death	Recovery
Wallau[58]	1942	22	i	0	Term	At term	Left	Survival	Recovery
Braz[4]	1943	42	iii	ii	Term	6 months after fetal death	Left	Death	Recovery
Casas[7]	1946	43	iii	ii	Term	9 months after last menstrual period	Right	Survival	Recovery
Ware[60]	1948	30	iii	ii	Term	15 months after term		Death	Recovery
Ross and Weeks[46]	1948	32		ii	Term	At term	Left	Survival	Recovery

Subsequent Pregnancies.—Several reports mentioned the occurrence of subsequent uneventful pregnancies. Notable among these are Osgood's[42] case cited by Jarcho in which the mother gave birth to six children while still carrying her abdominal tumor, and the case cited by Watters.[61]

TABLE III. TWENTY-THREE PROBABLE CASES OF TERM INTRATUBAL PREGNANCY COLLECTED FROM THE LITERATURE BY TITLE

AUTHOR	DATE	LENGTH OF GESTATION OR TIME OF LAPAROTOMY OR BOTH	FATE OF CHILD	FATE OF MOTHER
Pepin[43]	1892	7th month		
Lugeol[34]	1893	Gestation, 7½ months Laparotomy, 9½ months	Death	Recovery
Villar[57]	1894	Laparotomy, 12th month	Death	Recovery
Yakovleff[67]	1896	Gestation, term		Recovery
Fisher[18]	1902	Term	Survival	
Fisher[18]	1902	Term	Survival	
McGuire[35]	1904	Term		
Maes[36]	1905	Term		
Auguier[1]	1905	Term gestation Laparotomy, term	Death	Recovery
Barnsby[2]	1906	Gestation, term Laparotomy, 12th month	Death	Recovery
Masip[38]	1907	Term		
Fortacin[20]	1909	Term		
de Gouvea[14]	1917	Term		
Gentili[22]	1921	Term		
Probst[44]	1925	Term	Death	Recovery
Morgantini[40]	1929	Term		
Szlank[53]	1933	Term	Survival	
Gagnon[21]	1934	Term		
Uchida[55]	1935	Gestation, term Laparotomy, many years later	Death	Recovery
Werh[63]	1942	Term	Survival	
De Moura[15]	1942	Term	Death	Recovery
Infantozzi and co-workers[26]	1943	Almost term	Death	
Shannon and Heller[50]	1943	7 months	Death	Death

Cases Previously Reported

We have surveyed the literature and find that references to 44 cases of this unusual problem of pregnancy were available to us and that the existence of an additional 23 cases is probable because of the completeness with which the titles of the articles in which they are reported are recorded in the various indexing publications. We have made every possible attempt to be thorough in this survey but are well aware that cases of this condition have not been reported or that we have overlooked some reports. We have prepared two tables which give the available pertinent data in these cases. The 44 reported cases that we studied are listed in Table II and the cases which probably are instances of this condition but for which the entire report was not available are listed in Table III. In the cases included in Table II the criterion of no gross evidence of tubal rupture has been met and the condition either was or might have been handled by salpingectomy alone. Many cases were excluded because they did not meet these minimal criteria even though the titles of the articles suggested that intratubal term pregnancies without rupture of the tube had occurred.

The average age of the women afflicted concerning whom data were available was 30 years, the youngest was 19 and the oldest 43. In 8 of 28 cases in which data were available, the women had not previously borne children. In 35 of the cases, the duration of gestation was estimated to be at term, in 5 at eight months, and in 4 in the seventh month. There was an approximately equal distribution of these ectopic pregnancies in so far as right and left sides were concerned. Eleven (25 per cent) of the infants survived and 33 died. Thirty-nine (88.6 per cent) of the mothers survived and 5 died. If the cases in Table III are added to those of Table II, a total of 67 possible cases is obtained. We then know of an additional 9 fetal deaths and 4 cases in which the fetuses survived, making a grand total of 42 fetal deaths 15 fetal survivals and 10 cases in which the fetal outcome was not known. An over-all fetal mortality of 73.6 per cent is obtained. A maternal mortality of 11.3 per cent may be calculated on the basis of 47 surviving mothers and 6 maternal deaths. In 14 cases the maternal outcome is not known.

Report of Case

A primigravid woman, 28 years old, registered for examination at the Mayo Clinic on Sept. 14, 1949. Her early history was noncontributory and the menstrual history was normal. Her last menstrual period had been Oct. 6, 1948, and the expected date of confinement had been July 13, 1949. Prenatal care had been given elsewhere and the course of the pregnancy had been uneventful except for almost daily spotting until January, 1949, and one episode of dizziness without pain, vertigo, or collapse which occurred on Nov. 2, 1949. The patient had had no pain during her entire pregnancy. This point was particularly emphasized in the taking of the history when questions regarding the presence or absence of pain repeatedly produced the same answer. She had little nausea and vomiting during the first trimester of pregnancy. Her weight at the onset of the pregnancy had been about 115 pounds (52.2 kg.) and by July 1, 1949, had risen to 152 pounds (68.9 kg.) The patient was hospitalized elsewhere July 12, because of albuminuria, hypertension, and edema. The fetal heart tones were not heard then, and fetal movement had not been felt after July 8. The patient was hospitalized for eight days and the symptoms of toxemia cleared rapidly. Labor, however, did not occur. Accordingly, the patient was dismissed from the hospital and was not re-admitted until early August, 1949. At that time, after several unsuccessful attempts at medical induction of labor, two attempts at surgical induction were made and failed because of a hard and unyielding cervix. One of these surgical attempts was a bag induction. Neither attempt resulted in any labor pains whatsoever.

On admission to the Mayo Clinic in the middle of September, 1949, the patient stated that she had had occasional lower abdominal pain since the death of the baby with some suprapubic soreness. The breasts had regressed and the patient weighed 124 pounds (56.2 kg.) which was 26 pounds (11.8 kg.) less than when she had first been admitted to the hospital at home. She had had intermittent bloody discharge for the two months preceding admission and the last time that she had noted any blood had been about September 1.

Her blood pressure was 124/90 on admission, and the temperature and pulse were normal. General physical examination gave negative results except for generalized tenderness throughout the lower two thirds of the abdomen. The uterus was enlarged to about the size of that of a seven and one-half months' gestation. On rectal examination, the cervix was not at all effaced and was very firm. There was a curious lack of mobility to the entire pelvi-abdominal mass, which was completely inert and the fetal heart tones could not be heard. Clinically, it seemed as though the fetus was intrauterine in location.

The Aschheim-Zondek modification of the Friedman test gave negative results. A roentgenogram of the abdomen showed gross overlapping of the bones of the fetal calvarium and a shadow of uniform density surrounding the fetus that was presumed to be uterine wall. Roentgenographic examination of the thorax and urinalysis revealed nothing abnormal. The

erythrocyte count was 3,730,000 and hemoglobin was 72 per cent of normal (10.8 Gm. per 100 c.c.). The leucocyte count was within normal limits, but the blood sedimentation rate was 90 mm. at the end of one hour. Blood grouping tests revealed blood of group A, Rh negative.

Because both clinical and roentgenologic examination of the abdomen seemed to suggest an intrauterine pregnancy and because the history for an extrauterine pregnancy seemed lacking except for the failure to induce labor, a diagnosis of intrauterine fetal death with missed labor was made. The patient was given 25 mg. of stilbesterol each day for four days, and then medical induction of labor was tried; this consisted of administration of castor oil, quinine, and Pitocin and enemas. Abdominal hysterotomy was planned if induction failed. Further attempts at vaginal induction were decided against as was hysterosalpingography in view of the unfavorable cervix, and the history of previous intravaginal and intrauterine manipulation of considerable degree with markedly elevated blood sedimentation rate.

The medical induction failed, and, with the patient under nitrous oxide, oxygen, ethylene, and ether anesthesia, a lower midline incision was made. A reasonably sized peritoneal flap was turned for an operation in the lower segment of the uterus. The ''uterus'' was opened and a macerated female infant was extracted. There was almost no bleeding and the ''uterine wall'' was extremely atonic and colorless. The placenta could be only partially separated from the inferior surface of the sac. Because of this and because of the atonicity, hysterectomy was decided upon. There were many dense adhesions involving the small intestine, colon, and friable peritoneum; these were freed with extreme difficulty. When the ''uterus'' was completely freed, it became readily apparent that we had been dealing with the dilated left Fallopian tube. The uterus was approximately normal in size and the right adnexal area was negative. Accordingly left salpingo-oophorectomy was performed. The left ovary had, for all practical purposes, been destroyed by the pressure of the enlarging tube. This ovary was not involved in the formation of the sac wall but was nonetheless electively removed.

The postoperative course was without untoward events. The temperature rose to 99.5° F. on the second postoperative day and thereafter was not more than 98.6° F. The pulse rate rose to 100 beats per minute on the night of the operation and thereafter was normal. Dihydrostreptomycin, 2 Gm. per day, was given prophylactically for five days and penicillin, 400,000 units per day, was administered for a similar period. The wound healed uneventfully. The patient was dismissed from the hospital on the tenth postoperative day and left for her home a considerable distance away, one week later.

The specimen was studied carefully. The ovarian end of the Fallopian tube was dilated into a fibrous-walled cavity large enough to contain a fetus which weighed 2,600 grams and which was 49 cm. long. The placenta was approximately 15 cm. in diameter and was firmly attached to the inner and inferior surface of this cavity. Multiple sections were taken at widely separated sites from the wall of the sac and stained with both hematoxylin and eosin and van Gieson's stains. Smooth muscle was clearly demonstrated in the wall of the sac at multiple sites and at considerable distances from the normal, undilated tube. Ciliated columnar epithelium was noted at several sites relatively near the proximal, undilated tube.

Summary

We have reviewed the literature on intratubal pregnancies without rupture of the tube, occuring at or near term, and have endeavored to establish criteria by which the diagnosis of this condition may be made with precision. This variant of term ectopic gestation is of some importance and should be considered as distinct an entity as is primary ovarian pregnancy and abdominal pregnancy. Forty-five cases of this obstetrical rarity, including our own, were available for review. A fetal mortality of approximately 75 per cent and a maternal mortality in the neighborhood of 10 per cent were calculated.

Not all of the cases in our presentation have met the rigid criteria which we propose but in all cases of pregnancy listed in Table II there has, at least, been no gross evidence of tubal rupture and the condition was or would have been susceptible to complete extirpation by localized adnexal surgery.

Our primary purpose has been to establish a diagnostic yardstick for subsequent examples of this phenomenon.

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THE OBSTETRICIAN'S RESPONSIBILITY TO THE Rh-NEGATIVE PATIENT: THE MANAGEMENT OF THE Rh-SENSITIZED OBSTETRICAL PATIENT*

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IT IS now a clinically proved fact that the Rh factor has a definite relationship to erythroblastosis fetalis and serious or fatal transfusion reactions[1]; it is important for the physician dealing with the obstetric patient to understand and do adequate Rh tests on all prenatal patients.

A classification of Rh-incompatible matings† according to the potentiality of sensitization would enable the obstetrician to recognize which cases require limited rather than complete Rh investigation. To aid in the management of the patient during pregnancy as well as during delivery, a work sheet and hospital index card would assist the physician and hospital personnel in better supervision of the Rh-negative patient.

With standardization of the laboratory work-up on Rh-negative patients and proper management of these patients, it is possible to prevent accidental sensitization of mothers and to prevent unnecessary neonatal deaths due to erythroblastosis.

Preliminary Management of the Obstetrical Patient

In preparation for the management and classification of the Rh-negative patient we need to assemble certain facts routinely from all obstetric patients:

1. Obtain a complete obstetric and transfusion history, including abortions and possible intramuscular injections of blood.

2. Perform test for Rh factor at first visit on all prenatal patients, including primiparas.

3. If the patient is Rh negative, consult a competent Rh testing serologist for repeat examination, including Rh-Hr subgroups and A, B, O typing. If previous findings are confirmed, test the husband's and children's blood to determine the husband's genotype (homozygous or heterozygous for the Rh_0 factor).[2] The average laboratory cannot be expected to carry out the specialized serological studies necessary for this type of case. It is the obstetrician's responsibility to see that the indicated tests are done by a competent serologist and to collaborate with him throughout the entire antepartum, intrapartum, and postpartum periods.

4. Having found the patient with an Rh-incompatible mating, we attempt to classify her according to the potential or possible degree of sensitization now

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†The term Rh-incompatible mating is used throughout the paper in reference to the Rh-negative patient mated to an Rh-positive husband.

known. She should be reassured that, although alarming reports on the Rh
factor have been published, Rh-negative mothers for the most part bear normal
children and new tests and methods are available in the treatment of congenital
hemolytic disease.

Rh SENSITIZATION CLASSIFICATION

Class 0. Rh-compatible mating. Sensitization impossible.*

    A. Prospective mother Rh positive. Husband Rh positive or negative.
    B. Prospective mother Rh negative. Husband Rh negative.

Class I. Rh-incompatible mating. Sensitization improbable.

    A. Primipara with history negative for previous transfusion or intramuscular blood
       and with no history of abortions.
    B. Multipara with history negative and all children Rh negative.

Class II. Rh-incompatible mating. Sensitization potential.

    A. Primipara with history of previous abortion followed by negative antibody test.
    B. Multipara with history negative except for previous Rh-positive child or chil-
       dren, but antibody test negative near term or at one to three months post
       partum with previous pregnancy.

Class III. Rh-incompatible mating. Sensitization possible.

    A. Primipara with history negative except for previous induced abortion and
       antibody test not done.
    B. Multipara with history negative except for delivery of Rh-positive child and
       antibody test not done.

Class IV. Rh-incompatible mating. Sensitization probable.

    A. Primipara with history of possible previous isoimmunization:
       1. Transfusion of unknown or Rh-positive blood.
       2. Previous intramuscular injection of blood.
    B. Multipara with history of possible previous isoimmunization:
       1. Transfusion of unknown or Rh-positive blood.
       2. Previous intramuscular injection of blood.
       3. Delivery of an anemic, jaundiced, or of a spastic child.

Class V. Rh-incompatible rating. Sensitization positive.

    A. Primipara with history of previous isoimmunization and positive antibody test.
    B. Multipara with history of previous isoimmunization and positive antibody test
       in previous pregnancy; or delivery of an Rh-positive child with a positive
       Coombs test[3] or proved erythroblastosis; or a positive antibody test at one
       to three months post partum[4] or a positive antibody test in present pregnancy.

The mothers in Class O need only the laboratory work reviewed in the
preliminary management of obstetric patients. Those who are classified in
Classes I through V need further study in the way of antibody tests.

Antibody Tests

An antibody test should be done on Class I patients at 36 weeks. If the
titer at 36 weeks is negative, one test is sufficient during pregnancy. These pa-
tients remain in Class I for the present pregnancy. (A titer should be repeated
at four to eight weeks post partum on every woman with Rh-incompatible mat-

*Rh-positive women may become sensitized to factors other than Rh (Hr, A and B) and
produce a small percentage of the infants with erythroblastosis. With such obstetrical history,
patient should be in CLASS V.

ing delivered of an Rh-positive infant even though the child has no evidence of disease. If the postpartum titer is positive, the patient should be reclassified for a subsequent pregnancy.)

Classes II, III, and IV, as intermediate groups (potential, possible, and probable), should have antibody titers determined at 14, 24, 32, and 36 weeks, followed by a titer at 4 to 8 weeks post partum. If the fourteenth-week titer is positive, the patient should be reclassified in Class V. If positive on the succeeding test, she remains in Class V.

Patients in Class V should have antibody titers at 14, 20, 24, 28, 32, 36, and 38 weeks, and also at 4 to 8 weeks post partum.

In the presence of antibodies or increasing titers in the last trimester, arrange a consultation between obstetrician, pediatrician, and serologist, at 36 and 38 weeks, to decide whether the pregnancy should be terminated.

At present the ability to predict the occurrence and severity of erythroblastosis is relative rather than specific; however, Lucia and Hunt have recently attempted to evaluate the prediction factors. Their preliminary sampling showed that 45.4 per cent of those with antepartum sensitizations delivered infants with erythroblastosis, one-half of whom died of the disease.[5] Factors in order of importance are as follows: (1) blocking antibodies (albumin) higher than agglutinating (saline); (2) increasing antibodies during the last month before delivery; (3) "antibodies appearing earlier than 10 weeks before expected date of confinement; (4) presence of Rh antibodies in all successive testings after first appearance; (5) presence of ABO compatibility between mother and child. (This may be predicted if husband and wife are same ABO blood group or if husband is group O.)

"Although some normal Rh positive infants were born to mothers showing all five factors, in no instance did hemolytic disease occur when two or more of these factors were absent."[6]

The titer does not always bear a direct ratio to the severity of the disease; however, the higher the titer, the greater the likelihood for stillbirth in the Rh-positive fetus. Induction of labor before intrauterine death occurs, if the infant is viable, may yield a baby which can be treated.[7]

Indications for Induction of Labor

Induction of labor at 37 to 38 weeks may be indicated if there is: (1) Rh-incompatible mating with potent antibodies increasing in the thirtieth to thirty-sixth week; (2) history of previous erythroblastotic baby or transfusion with Rh-positive blood; (3) presumably homozygous husband.[2]

Before termination of the pregnancy in the presence of the above indications, adequate x-ray study of the fetus in utero should be done to insure the presence of a live fetus as well a to determine the maturity of the baby for probable survival.

X-ray study of the fetus in utero may show soft tissue changes in the hydropic fetus with a halolike appearance about the skull from edema. The hydrops causes the infant to assume a Buddha-like position in utero.[8] Enlargement of the spleen and liver, as well as increased bone density, may also be seen. This x-ray study may aid in avoiding cesarean delivery of a hopelessly damaged or stillborn hydropic infant. One of the earliest signs of fetal death is overlapping of the skull bones, while later one may see sharp angulation of the head in relation to the spine, lordosis of the caudal portion of the spine, collapse of the thoracic cage, or generalized decalcification.[9]

Indications for cesarean should be based primarily on adequate obstetric rather than serologic findings. Wiener and Wexler have recently submitted a

preliminary report showing 50 per cent higher mortality rate in infants delivered by cesarean.[10]

When interruption of pregnancy is finally contemplated, if the presenting part is engaged, a sterile vaginal examination with artificial rupture of the membrane is recommended as a means of determining the color of the amniotic fluid. The presence of yellow or amber amniotic fluid implies more severe disease in the infant than does clear fluid. If the cervix is ripe, a trial of labor should be justified.

Management at Time of Delivery

The sensitized Rh-negative patient should be delivered in a hospital with adequate laboratory facilities, including a blood bank with at least three pints of Type O Rh-negative blood on hand, or suitable donors present, for immediate replacement of blood volume of either the mother or of the infant. A pediatrician and competent laboratory personnel should be present and immediately available to the delivery room. Team work is necessary for early diagnosis and treatment in saving more of these infants.

At birth, physical findings of yellow amniotic fluid, large pale placenta, golden vernix caseosa, splenomegaly, jaundice, or anemia in a baby whose mother has a typical history, or serologic picture, of Rh sensitization are sufficient evidence of actual disease and indication for immediate treatment.[11] Upon delivery, doubly clamp the cord early several inches from the abdominal wall in the event that the cord need be catheterized for withdrawal of blood at exchange transfusion. Do not remove clamp from placental attachment of cord. This procedure will prevent delay and inconvenience of venipuncture of infant. Obtain 10 c.c. of oxalated cord blood by venipuncture of a distended vein on the fetal surface of the placenta, using dry syringe and needle. Do not remove the placenta manually or express forcibly.

Diagnosis of Erythroblastosis

Laboratory tests on cord blood aid in early diagnosis of erythroblastosis and should be done on all newborns of Rh-incompatible matings in the following order:

1. Coombs test: A positive Coombs test is considered pathognomonic of hemolytic disease in the newborn, and may indicate the severity.[12] (It will also be positive in a small percentage of the infants with erythroblastosis delivered of Rh-positive mothers.[2])

2. Hemoglobin: The cord hemoglobin is perhaps the most reliable index of severity of hemolytic disease in comparison with the maternal or fetal antibody titers.[13]

3. Rh determination and blood typing: Occasionally at birth a false Rh-negative report will be made "due to the blocking action of the maternal antibody, but a positive Coombs test will demonstrate that the cells have been sensitized in utero and that the infant is really Rh positive."[14]

4. Cell count and smear for nucleated red blood cells.

5. Icterus index (optional in the absence of jaundice).

Management of Erythroblastosis

Many babies with a mild erythroblastotic process will survive without transfusion. Some infants may appear normal at birth, but will develop jaundice or anemia after several days or weeks; however, a direct positive Coombs test at birth should forewarn the pediatrician. A 10 to 30 per cent incidence of neurologic sequelae, such as mental retardation, athetosis, cerebral palsy, hearing defects, and the like, has been reported.[15] Some authorities have felt

that these neurologic complications developed in utero and that no treatment after birth would alter these complications. However, a few reports after the first two years' experience with exchange transfusion suggest a lower incidence of brain damage.[7]

It is of prime importance that transfusion, when indicated, be given as soon as the blood tests are reported. Sufficient blood should be given to insure temporary correction of the anemia and proper maintenance of blood volume. An exchange transfusion may be decided upon by the consulting pediatrician when there is evidence of moderate or severe erythroblastosis. In any event, the physician should be prepared to have multiple transfusions given skillfully during the next month or six weeks as needed. Rh-negative specific type blood should be used. Allen, Diamond, and Watrous have recently reported a 50 per cent greater survival of infants receiving blood from nonsensitized women donors than from men.[16] The baby's mother should not be used as the donor. In severe cases of erythroblastosis, the infant should be kept warm and in an oxygen-supplied incubator. If the facilities are inadequate for the treatment of erythroblastosis fetalis in the hospital where delivery occurs, there should be no delay in transferring the baby to a properly equipped institution.

Work Sheet

Since the management of the Rh-negative patient includes a number of laboratory tests which should be done at definite intervals, it would seem advisable to have a work sheet attached to the patient's record at the time of her first prenatal visit, which would accommodate all necessary classification and testing throughout her prenatal and postpartum care.

A work sheet has been devised which includes Rh classification of all prospective mothers, minimal laboratory tests required for each classification, and laboratory testing for the newborn of the Rh-negative patient. The purpose of the work sheet is to act as a constant reminder to the physician of the Rh factor and its role in erythroblastosis; to help establish Rh testing of all prospective mothers; to aid in the standardization of minimal laboratory testing on Rh-negative mothers; to insure adequate testing of the infants of the Rh-negative patient; and to provide a permanent record for the test findings.

Rh Negative Card

Further to insure adequate awareness of the Rh-negative patient, the use of an index card is suggested to be sent to the hospital for filing on the delivery floor on or before the sixth month of gestation. This Rh-negative card would be attached to the front of the patient's chart on admission to the hospital. It should be a conspicuous color, namely pink, so that it will be readily seen by all concerned with the patient's care.

Rh NEGATIVE CARD

Name: Jones, Mrs. John (Susan)   EDC _____
Address: _____

    Rh sensitization classification

    Patient referred to Rh Consulting Laboratory

    Husband referred to Rh Consulting Laboratory

_____ M.D.

WORK SHEET

MINIMAL LABORATORY REQUIREMENTS. INDICATIONS FOR FOLLOW-UP TESTS

Rh ALL PATIENTS ON FIRST PRENATAL VISIT					
Rh patient (If positive, no further tests)	Neg.		Pos.		
Rh husband: (If positive*) (If negative, no further tests)	Neg.		Pos.		
Rh positive husband: Subgroup tests					
Rh children when: (Mother is Rh negative) (Father is Rh positive)	1st	2nd	3rd	4th	
Rh positive husband's genotype is:	Heterozygous				
	Homozygous				

*Rh laboratory shall confirm test and do all further testing.

CLASSIFY ALL Rh-NEGATIVE PATIENTS. (CLASSIFICATION AS GIVEN UNDER ''PRELIMINARY MANAGEMENT'' TO BE PRINTED ON REVERSE SIDE.) MAIL Rh-NEGATIVE CARD TO HOSPITAL FOR FILING ON THE DELIVERY FLOOR.

		ANTIBODY TITERS*							
WEEK OF GESTATION†		14	20	24	28	32	36	38	4-8 POST-PARTUM
CLASS 0	Neg. Pos.								
CLASS I	Neg. Pos.						....		....
CLASS II‡ III IV	Neg. Pos.	....		....		....	....		....
CLASS V	Neg. Pos.	....	....	....	....	....	....	....	....

*If patient has a positive antibody titer, she should be delivered in a hospital with facilities for Rh and Coombs testing of infant; a pediatric consultant should be ready to give exchange or multiple small transfusions.

†Titer to be done where spaces are indicated.

‡When an antibody test is positive (Classes I, II, III, IV) reclassify patient to Class V. If negative test, proceed as indicated for each class.

TESTS FOR ALL INFANTS OF PATIENTS IN CLASSES I THROUGH V

Obtain 10 c.c. oxalated cord blood	
Coombs test	
Rh (blood typing as indicated)	
Blood count and hemoglobin	
Smear	
Icterus index (as indicated)	

Comment

The importance of routine testing for the Rh factor in the prospective mother has been acknowledged since the supply of serum has become universally available. Because there is now greater likelihood of a newborn having erythroblastosis than congenital syphilis, the obstetrician should consider the minimal laboratory requirements for every Rh-incompatible mating. The classification and work sheet will assist him in the management of each patient, especially when one realizes the economic factor involved, were he to request monthly antibody titers for 13 per cent of all his obstetrical patients.[17] Actually less than 1 per cent of obstetrical patients fall into Class V, the only group requiring extensive laboratory study. Furthermore, it is becoming my belief that we can

safely delete the twenty-fourth week antibody titer for the intermediate group (Classes II, III, and IV) and the twentieth and twenty-fourth week titer for Class V. Even with these deletions, we can detect initially the few with prior isoimmunization, and later recognize which cases develop antibodies before or after the thirtieth week.

Although we have no specific treatment for the prevention of erythroblastosis, the obstetrician who ignores the problem of the Rh-incompatible mating may at some time be vulnerable to medicolegal action by a vindictive patient. Such action in some cases with fetal death or irreparable brain damage could be based upon delay in the diagnosis and treatment, as well as failure to test for the Rh factor in the mother. Since the adoption of the classification and the work sheet by the Obstetrical Staff of St. John's Hospital, Santa Monica, Calif., they have enabled the obstetrician to evaluate the situation at the time of the initial consultation as well as collaborate with the pediatrician.

Since patients only temporarily remain in Class III or IV, and subsequently, revert to either Class II or Class V, there are actually only three major groups other than the control group, Class O, as outlined on the work sheet. Thus the primary classification may be condensed as follows:

GROUP I. Improbable sensitization. Prospective mother Rh negative with history negative for possible previous isoimmunization, and all children, if any, Rh negative.

GROUP II. Potentially sensitized. Prospective mother Rh negative with history of possible previous isoimmunzaton or prevous Rh-positive child, but antibody test negative approaching or following termination of previous pregnancy, and currently negative in present pregnancy.

GROUP III. Sensitized. Prospective mother Rh negative, isoimmunized, with positive antibody test in previous or present pregnancy. Group III may be subdivided into IIIA, husband heterozygous; and IIIB, husband homozygous.

It is my hope that this classification will be comparable in value to the obstetrician to Pardee's functional classification of heart disease.[18] Certainly we no longer worry or advise against pregnancy in the woman with minimal cardiac findings that may be evaluated as Class I or II, while those patients who are Class III or IV cardiac patients deserve entirely different prognosis and treatment.

Summary

The management of the Rh-negative patient during pregnancy has been discussed. A classification has been suggested to determine the minimal laboratory requirements necessary for individual patients, thereby aiding in the possible prediction of erythroblastosis fetalis. A work sheet has been presented to aid the physician in deciding the amount of laboratory work necessary for individual patients. A method in the form of an index card has been suggested to warn the delivery room staff of Rh-negative patients to be admitted to the hospital. The immediate management of the newborn to determine the presence of erythroblastosis has been outlined and a choice of treatment suggested.

Until specific treatment of the Rh-negative mother has been developed for the control of erythroblastosis in infants, it would be advisable to examine all Rh-negative patients systematically and to provide laboratory and hospital facilities in order to improve the survival rate of their infants.

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MALIGNANT LESIONS OF THE UTERUS ASSOCIATED WITH ESTROGEN-PRODUCING OVARIAN TUMORS

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THE coexistence of uterine carcinoma and functioning or feminizing ovarian neoplasms has been observed by several writers[1-5] and, in 1939, MacCarty and one of us (Dockerty[6]), in a report on some of the first cases, suggested the possible importance of estrogen as the carcinogenic agent in operation. Novak and Yui[7] at Johns Hopkins Hospital are currently preparing a report on the subject and we propose at this time to outline briefly our singular experience.

In a study of 87 granulosa-cell and theca-cell tumors[8,9] we have noted the occurrence of uterine cancers 15 times; no less than 3 of these patients have had mammary carcinoma (bilateral on one occasion). The over-all incidence of the association of uterine and ovarian lesions was more than 15 per cent, and the figure reached 27 per cent when considered as the percentage of patients who suffered the complication, if such you will allow us to call it, after the age of 50 years. Uterine cancer did not complicate granulosa-cell and theca-cell tumors of younger women. This observation is important as we shall see later from the standpoint of treatment.

Report of Cases

In the following brief reports of cases we shall attempt to summarize the salient features which are pertinent to the discussion.

CASE 1 *(Previously reported by Dockerty and MacCarty).*—A white woman, gravida iii, para i, had a delayed menopause at the age of 54 years, two years of amenorrhea, and then more or less menstrual-like bleeding for one year. Material removed by curettage showed endometrial hyperplasia and radium was inserted. Amenorrhea followed for three years and then irregular spotting occurred for six months. She was thought to have fibroids, but at hysterectomy she was found to have a granulosa-cell tumor of the right ovary, 8 cm. in diameter. The left ovary was atrophic. The uterus was symmetrically enlarged and the endometrium showed noninvasive adenocarcinoma, Grade 1. The patient was living and well seven years later.

CASE 2 *(Previously reported by Mussey, Dockerty and Masson)*[10].—A woman, 46 years of age and the mother of seven children, reported that in 1940, at the age of 39 years, she had been given a dose of radium for excessive fertility and for three years she enjoyed amenorrhea, without morning sickness. Three years before her admission to the clinic bleeding recurred, regularly at first, then irregularly, and finally continuously for several months. She became concerned.

On examination a fungating mass was found in the vagina which, it was ascertained, arose from the fundus rather than from the cervix. Hysterectomy revealed sarcoma of the endometrial stroma, Grade 4, and areas of uterine adenocarcinoma, Grade 3. An

adenomyoma was found incidentally. The left ovary was the seat of a malignant theca-cell tumor which measured 7 by 6 by 4 cm.

CASE 3.—In 1937 a woman, gravida i, para i, and 46 years of age, underwent radical mastectomy on the right side for adenocarcinoma, Grade 3, with normal nodes. She had had menorrhagia for fourteen years. It was thought that she had fibroids, and she was given a menopausal dose of radium to control bleeding. Six years later she came back to have the left breast removed for an adenocarcinoma, Grade 3, with involvement of one node. She gave a history of a vaginal discharge of several years' duration.

The uterus seemed to be larger than it had been on previous visits. At operation what was thought to be a large uterus proved to be a granulosa-cell tumor which weighed 1,000 Gm. The uterus itself weighed 100 Gm. and was the seat of an adenocarcinoma, Grade 1. The patient is living and free from all 3 carcinomas six years after the last operation.

CASE 4.—A nulliparous woman, 59 years of age, was seen at the clinic in October, 1930, because of menorrhagia and metrorrhagia of five years' duration. A mass in the pelvis was thought to be an enlarged uterus, and hysterectomy was advised. At operation it was found that the uterus was the seat of a diffuse adenocarcinoma, Grade 2, which involved the fundus and invaded the myometrium to a depth of 2 cm. It weighed 130 Gm. The left ovary was atrophic and the right contained a granulosa-cell tumor 2 cm. in diameter. Fifteen years later the patient died, apparently from unrelated causes.
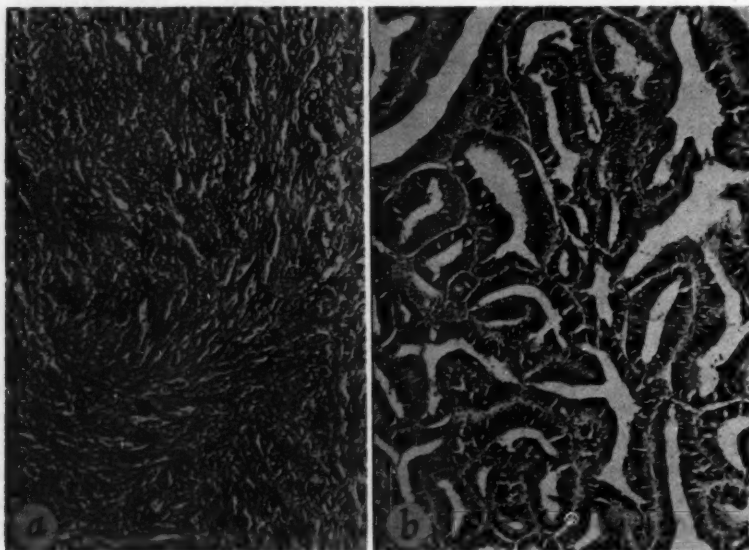
Fig. 1 (Case 7).—a. Section from right ovarian tumor showing the spindle cells arranged in whorls. (Hematoxylin and eosin, ×200.) b. Endometrial adenocarcinoma, Grade 1. The lack of stroma and the "back-to-back" arrangement of the glands are typical. (Hematoxylin and eosin, ×55.)

CASE 5.—A nulliparous woman 48 years of age presented herself at the clinic in February, 1923, with the complaint of menometrorrhagia. Seven years previously her menses had ceased. Eight months previous to her admission they had recommenced. Bleeding was profuse and prolonged with an evershortening interval between periods. The uterus seemed to be enlarged. At operation it was found to be the seat of a diffuse noninfiltrating papillary adenocarcinoma, Grade 2. A granulosa-cell tumor 2 cm. in diameter involved the right ovary. The patient died nineteen years later apparently from an unrelated cause.

CASE 6.—A 60-year-old woman, para iii, gravida iii, complained of semiperiodic vaginal bleeding and discharge of nine months' duration. Menopause had occurred at the age of 52 years. A pelvic mass was felt and the possibility that it was a granulosa-cell tumor was considered. Curettage was positive for adeno-acanthoma, Grade 1; hysterectomy was performed and a growth which measured 3 by 2 by 1 cm. was removed from the right side of the pelvis. Fibromyomas also were present. The left ovary was atrophic and the right showed a yellowish, solid theca-cell tumor, 1.5 cm. in diameter. Follow-up letters have not been mailed to her at the time of this report.

CASE 7.—A 61-year-old woman, gravida iii, para iii, complained for ten years of semiperiodic vaginal spotting which had occurred after fifteen years of amenorrhea. The uterus seemed enlarged. Curettement revealed adenocarcinoma of the fundus, Grade 1, and hysterectomy was performed. The uterine growth measured 8 by 8 by 2 cm. Both ovaries were sites of theca-cell tumors, each of which measured 3.5 cm. in diameter (Fig. 1). Death from unrelated causes occurred four years later.

CASE 8.—A woman, gravida iii, para i, who was 53 years of age, complained of postmenopausal spotting which lasted for ten days. Her menstrual history had been normal and her menopause at the age of 47 years without incident.

Biopsy of the cervix showed the presence of epidermoid carcinoma, Grade 2, and since the lesion appeared to be small, it was decided to perform a Wertheim hysterectomy. The lesion measured 2 by 2 cm. and extended to a depth of 1 cm. The nodes were not involved. Uterine fibromyomas were present and the endometrium appeared atrophic. A theca-cell tumor, yellowish in color and 1 cm. in diameter, involved the left ovary. The patient was living and well nine years later.
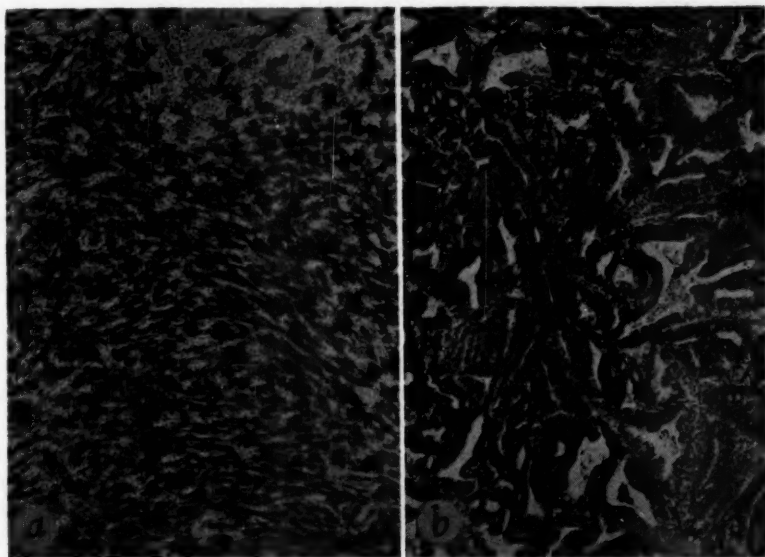
Fig. 2 (Case 9).—a. Theca-cell tumor of the left ovary. The lipoid-laden spindle cells are plumper than those usually seen in fibromas. (Sudan III, ×200.) b. Endometrial adenocarcinoma exhibiting the typical features of a lesion of Grade 2 according to Broders' classification. (Hematoxylin and eosin, ×55.)

CASE 9.—A white woman, gravida iii, para iii, 58 years of age, complained of vaginal spotting with bright red blood which had occurred for one month. Menopause had occurred at the age of 46 years. Curettement revealed an adenocarcinoma of the endometrium, Grade 2; hysterectomy was performed and the growth 6 by 3 by 1.5 cm. was seen to infiltrate the myometrium (Fig. 2). In the right ovary there was a low-grade malignant theca-cell

tumor which measured 2.5 cm. in diameter; the left ovary was atrophic. Fourteen years later this patient wrote that her condition was good except for "high blood pressure."

CASE 10.—Five years after a normal menopause at the age of 52 years, a primiparous white woman underwent an emergency operation for malignant theca-cell tumor of the right ovary. The tumor, which measured 11 by 9 by 8 cm., was on a twisted pedicle. The uterus, which was not disturbed, was said by the surgeon to be enlarged and to contain multiple small fibromyomas. The patient was treated postoperatively with intrauterine radium. Eight years later adenocarcinoma, Grade 3, developed in the cervical canal and was treated by insertion of radium. Death from metastasis ensued six years after discovery of the cervical lesion.

CASE 11.—A single white woman, 65 years of age, had suffered from intermittent post-menopausal vaginal bleeding. The uterus contained fibromyomas and also an adenocarcinoma of the endometrium, Grade 2. A theca-cell tumor 2 cm. in diameter involved the left ovary; the right ovary was atrophic.

CASE 12.—A nulliparous white patient, 70 years of age, complained of irregular vaginal spotting of four years' duration and of signs of myxedema of fifteen years' duration. Her last menstrual period had occurred at the age of 35 years after a pelvic operation for what was said to be an ovarian cyst. Curettement showed evidence of adenocarcinoma, Grade 2, and at hysterectomy the fundal growth measured 4 by 3 by 1.5 cm. Two fibromyomas also were present. The right ovary was absent and the left ovary was the seat of a typical granulosa-cell tumor 4.5 cm. in diameter. The patient was living and well fourteen years later.

CASE 13 (Previously reported by Mussey, Dockerty and Masson)[10].—The history of this patient will be given in greater detail since, as with the first 3 cases presented, it brings into focus the possibility that ovulation may play a part in the histogenesis of the ovarian tumors. A 64-year-old white woman had undergone treatment with roentgen therapy for fibroids before her admission to the clinic. Her menses ceased and the tumors shrivelled, but an intractable actinodermatitic ulcer developed on the suprapubic area. Fifteen years later episodes of vaginal bleeding ensued which were partially controlled with radium. She came to the clinic five years after this because of recurrent vaginal bleeding.

Significant physical findings were a pelvic mass and an indolent ulcer 8 by 5 cm. located just above the pubis.

The operative findings consisted essentially of adenocarcinoma and leiomyosarcoma of the uterus and a metastatic granulosa-cell tumor of the right ovary. We are not claiming that the basosquamous-cell carcinoma which this patient had in the anterior abdominal wall was related etiologically to the estrogen produced by the ovarian tumors, but it certainly points up still another unusual feature in this most unusual case. The patient died shortly after operation as was to be expected.

By way of comment we can state that the association of endometrial carcinoma with feminizing ovarian tumors is perhaps 100 times as frequent as would obtain on the basis of chance alone. Inquiry as to the possible pathogenesis of the endometrial lesion brings to mind at once the estrogenic factor since it is in the production of this hormone that granulosa-cell and theca-cell tumors differ from other neoplasms of the ovary. We find that a number of sources furnish evidence for our contention that estrogen does in fact play an important role in the development of uterine carcinoma.

CASE 14.—A single white woman, 49 years of age, registered at the clinic in 1933 with complaints referable to hypertension and beginning cardiac decompensation. The menstrual history was apparently normal except that menometrorrhagia had been present for two months. On examination there was marked obesity, hypertension, cardiac enlargement, and chronic venous congestion with fluid in the right portion of the thorax. Pelvic examination revealed a right adnexal mass.

Thoracentesis was performed on the right, and the cardiac status of the patient improved with the use of diet and drugs. One month after admission laparotomy was performed for a cystic granulosa-cell tumor, 18 cm. in diameter, which involved the right ovary. Both ovaries and both tubes were removed but the uterus was not disturbed because of the added risk entailed. The surgeon evacuated a considerable amount of ascitic fluid. She returned two years later because of a bloody vaginal discharge of four months' duration. Prior to that and since the time that laparotomy was performed she had had amenorrhea. Dilatation and curettage revealed adenocarcinoma of the fundus, Grade 1, and it was elected to treat the patient with radium in view of her precarious cardiac condition.

In 1944 the patient was admitted to the clinic because of a lump in the right breast which had first been noted four months previously. Radical mastectomy was performed after preliminary biopsy showed evidence of scirrhous adenocarcinoma, Grade 4. The growth measured 4 cm. in diameter and there was metastatic involvement of one axillary node.

Subsequently diabetes developed and the patient returned on several occasions for regulation of this and because of her chronic congestive heart failure. In spite of all her difficulties she was living and ''cancer free'' five years after the operation on her breast.

Case 15.—A 61-year-old white woman, para x, gravida x, registered at the clinic in 1910 complaining of prolapse of the uterus. Menopause had occurred at the age of 43 years.

For sixteen years she had suffered from prolapse of the uterus which had been partially controlled by the use of a pessary. Vaginal bleeding accompanied by a foul discharge had been present for one month. On examination the uterus was found to be enlarged and was thought to contain fibromyomas.

At hysterectomy the uterus was found to be the seat of a diffuse noninfiltrating adenocarcinoma, Grade 1. A partly cystic and partly solid encapsulated granulosa-cell tumor was present in the right ovary which measured 15 cm. in diameter; the left ovary was atrophic.

Six years later the right breast was removed elsewhere because of a scirrhous carcinoma with extensive axillary nodal involvement; death occurred in 1920 from the effects of metastasis.

Although we have been unable to obtain tissue or slides from the mammary lesion, the lapse of six years between its development and that of the uterine carcinoma makes the case a clear-cut example of multiple primary carcinomas associated with granulosa-cell tumors.

While this manuscript was being prepared our colleague, Dr. William Dick of Parkersburg, W. Va., provided us with information from an additional case of granulosa-cell tumor of the ovary and endometrial carcinoma, and generously allowed us to include it in our report.

Case 16.—A woman, 63 years of age, had complained of postmenopausal bleeding. The uterus seemed to be enlarged. Material removed by curettage was positive for adenocarcinoma of the fundus, Grade 1, and at hysterectomy a ruptured cystic granulosa-cell carcinoma was unexpectedly encountered. Follow-up studies are not available at the time of this report.

Comment

Experimentally there are two related pieces of evidence. Gardner and co-workers[11] have induced carcinoma-like lesions in the cervices of mice receiving estrogens. Greene[12] observed a high incidence of metastasizing fundal carcinomas in old multiparous rabbits whose livers had been markedly impaired by repeated attacks of ''toxemia of pregnancy'' so that breakdown of circulating estrogens no longer occurred. It appears, however, that fundal carcinoma

rarely occurs in experimental animals other than in rabbits of that group already mentioned, and this may account for the difficulty of inducing the lesions in other species through the administration of exogenous estrogens.

On the clinical side it has been noted that uterine as well as mammary carcinomas are rarely observed after oophorectomy[9] even though the adrenal glands continue to supply estrogen in small amounts. On the positive side of the picture Speert[13] noted a high incidence of fundal carcinoma among patients suffering from cirrhosis of the liver. He felt that the liver had stopped its breakdown of estrogens and was responsible for a high concentration of circulating hormones which exerted a carcinogenic effect among susceptible individuals. In the Middle West where women live closer to the soil than to the bottle it is difficult to secure any sizable series of cirrhotic patients to test the validity of his claim.

Along the same line but more nebulous is the notion that dietary deficiency in the vitamin B complex might operate by producing subclinical hepatic dysfunction. Ayre and Bauld[14] entertained this notion when they found degrees of thiamine deficiency among 20 patients suffering from carcinoma of the fundus.

Perhaps more positive were the observations also of Ayre and Bauld[14] that vaginal smears of a group of women with malignant uterine lesions showed sustained estrogenic activity. As a corollary Randall[15] and others have noted that patients with fundal carcinomas enjoy a late menopause featuring symptoms that are unusually mild.

Fremont-Smith and his associates[16] report the case of a woman, 43 years of age, who accidentally had received almost 12,000,000 rat units of estrogen over a period of eight years because of severe menopausal symptoms. Serial samples of endometrium removed by curettage during the eight years showed the development from endometrial hyperplasia to carcinoma. One swallow does not make a summer, but in view of this and the other evidence presented it might be well to question the harmlessness of endogenous or exogenous estrogen circulating in excessive amounts.

The association, in three instances, of a ''feminizing'' ovarian tumor with carcinoma of the breast as well as of the endometrium brought out still another feature of interest in our study. In an independent investigation carried out in the laboratory of one of us (Dockerty), McVicker[17] found mammary and uterine adenocarcinoma coexisting in 46 cases; he ascertained from figures of incidence that this number was 2.4 times as great as would obtain on the basis of chance alone. In our study we found that if granulosa-cell and theca-cell tumors of the ovary were added to the combination of coexisting mammary and uterine adenocarcinomas the number of cases would show an eightfold further increase (about 17 times) over what would obtain on the basis of chance alone. Allen[18] and Auchincloss and Haagensen[19] have emphasized the importance of estrogen in the induction of mammary carcinoma. Nathanson,[20] on the other hand, has pointed out that the administration of estrogens to patients having advanced cancer of the breast may produce beneficial changes, especially if involvement of soft tissue predominates and if the patient is more than 60 years of age.

Summary and Conclusions

A series of 16 cases is presented in which functioning (feminizing) ovarian tumors were associated with the presence of uterine carcinoma. The association was much more frequent than that which could be explained on the basis of chance alone.

Carcinogenic influence of estrogen is suggested as a possible cause.

The prevalent literature on the subject is reviewed briefly.

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SECONDARY MALIGNANT DISEASE OF THE OVARIES

A Study of 72 Autopsies

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THIS is a study of the frequency, age incidence, site of origin, method of spread, and other features in secondary malignant disease of the ovaries, made from the autopsy records and slides of the University of Toronto and the clinical histories of the Toronto General Hospital.

During the twenty-five year period from 1925 to 1949, 10,287 autopsies on both sexes were performed at the Banting Institute. Of these, there was secondary neoplasm in one or both ovaries in 72 cases, an incidence of 0.7 per cent. In contrast with our figures, Hundley[3] found only 11 cases of metastatic carcinoma in 11,200 autopsies at the Johns Hopkins Hospital.

In the majority of cases we were able to make a reasonable assumption as to whether the secondary tumor in the ovary was metastatic or the result of direct

TABLE I.

ORGAN	NO. OF CASES OF SECONDARY TUMOR IN OVARY		NO. OF CASES OF PRIMARY TUMOR		PER CENT INVOLVEMENT OF OVARIES
Group 1.—					
Breast	18		158		12.2
Lung	2		157		1.28
Meninges of brain	1				
Group 2.—					
Stomach	8		204		3.9
Colon (hepatic flexure)	1				
Liver	1				
Gall bladder	1				
Kidney	1				
Group 3.—					
Cervix uteri	13	3 metastatic 10 direct	148	2.0%	8.8
Fundus uteri	6		44	6.8%	14.0
Ovary	3				
Cecum	2				
Sigmoid	2				
Rectosigmoid	2				
Rectum	3				
(Total large gut)	(10)				
Ureter	1				
Group 4.—					
Lymphosarcoma	4				
Reticulum cell sarcoma	1				
Fibrosarcoma	1				
Adenocarcinoma of unknown origin	1				
Total	72				

extension. The ovarian tumors were known to be metastatic in 53 cases. In the remaining 19 cases the secondary invasion was mostly by direct extension, although in some cases the lesion was so extensive that the method of spread could not be ascertained.

In Table I the derivation of the ovarian tumors is analyzed and compared with the total incidence of tumor in the corresponding primary sites. The reason for the arrangement of the various organs into four groups will be discussed later.
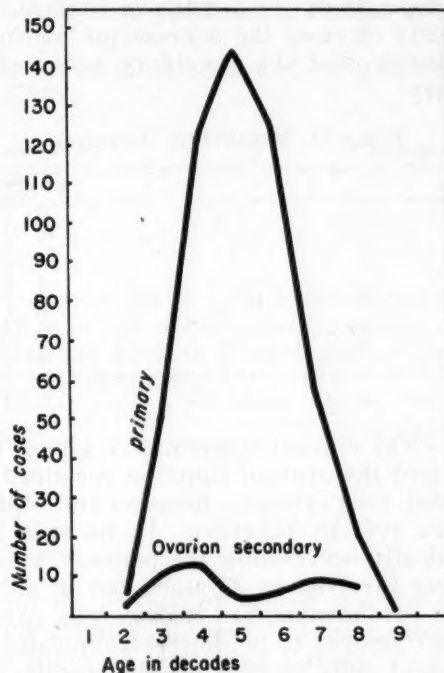
Fig. 1.—A comparison of the age incidence of the ovarian secondaries with that of the tumors of the primary sites.

Age.—The general age distribution was between 22 and 78 years, with an average of 50.1 years. Table II shows that of 48 cases of metastatic carcinoma, there were 29 in the third, fourth, and fifth decades and 19 in the sixth, seventh, and eighth decades, indicating that metastases occur sufficiently often after the age of the menopause to make them worthy of consideration. Fig 1 compares the age incidence of ovarian secondaries with that of the tumors of the primary sites. The peak in the primary tumors is in the fifth decade and is still high in the sixth decade. In the secondary tumors the peak is in the fourth decade and is low in the fifth and sixth. This difference is insignificant when the figures are compared statistically.

Side Involved.—As in most of the statistics, the malignancy was bilateral in 62 per cent of the cases, and in the remaining cases it occurred an equal number of times in each ovary. Willis,[8] however, found that in the unilateral cases the right ovary was much more frequently involved.

Gross and Microscopic Features.—In 37 cases (slightly more than half) the ovary was not grossly enlarged and the metastatic lesion was found only on microscopic examination. The importance of this is realized when it is known that in some autopsies the ovaries are not examined if no gross pathologic change is evident and the incidence of secondary ovarian involvement given is therefore

too low. The ovaries should be routinely examined microscopically in all cases of malignant disease that come to autopsy, and the surgeon at operation should not be misled into a false sense of security if he finds the ovaries of normal size. Sometimes the enlargement of the ovary was due chiefly to the presence of a benign cyst and enlargement due to secondary tumor was a prominent feature in but few cases.

If visible, the tumors are usually solid and firm and may contain areas of degeneration. In some cases scattered tumor nodules are seen, and in others the tumor consists of deposits on the peritoneal surface.

In the great majority of cases the microscopic picture was very similar to that of the primary tumor, but the secondary lesion often had more fibrous stroma than the primary.

TABLE II. METASTATIC CARCINOMA

DECADE	NUMBER OF CASES	
2	3	
3	10	
4	12	29
5	4	
6	5	
7	8	19
8	6	
Total	48	

Clinical Features.—The clinical symptoms in almost all the cases were due to the primary lesion, and the ovarian function remained undisturbed or gradually diminished. Indeed, even extensive invasion and replacement of the ovaries failed to interfere with ovarian function. In no case in this series did the ovarian metastases clinically overshadow the primary lesion.

The peritoneum was involved in 27 cases, but in only 10 of these was the picture that of diffuse carcinomatosis. Ascites was present in 47.3 per cent (34 cases) in a sufficient amount to be detected clinically. Examination of the ascitic fluid for malignant cells yielded positive results in only a few of the cases in which it was performed.

Frankl,[2] in discussing the method of metastasis, classified the primary malignancy in three groups:

1. Those which have no topical relation to the ovaries (breast, thyroid, etc.).
2. Those which have a partial topical relation (stomach, liver, gall bladder, intestines, etc.).
3. Those which have a close relation to the ovaries (uterus, tubes, rectum, etc.).

To these we have added a fourth "General Group" and divided our cases accordingly to facilitate discussion. The cases in Table I have therefore been arranged accordingly.

Group I (No Topical Relation to the Ovaries)

A. Breast.—Statistics by various authors differ greatly as to the frequency of metastases from the breast to the ovary. Novak[5] states that this occurs only occasionally; others report that it is second in frequency to the gastrointestinal tract, while Stengel and Fox[7] state the breast is the most common primary site. Paget[6] found metastases in the ovaries in 5 per cent of 735 cases of cancer of the breast.

In this series, 18 of the tumors were derived from the breast, an incidence greater than from any other single organ and equal to that of all the organs

of the gastrointestinal tract combined. The total number of cases of breast carcinoma that came to autopsy during the same period was 148, making the percentage of metastases to the ovaries 12.2.

The average age in which the primary tumor occurred in the breast (Table I) was 56 ± 1.1 years and the secondary 46.2 ± 8 years; the statistical difference is highly significant, the probability of its occurring by chance being only 0.1 per cent. This is the only organ in which we find justified the common belief that secondary carcinoma from the ovary is commoner before the menopause. The analysis of the other sites of primary carcinoma does not show this relationship.

Both ovaries were involved in 11 cases and were enlarged in 9. The microscopic picture was as follows:

MICROSCOPIC TYPE	NUMBER OF CASES
Medullary carcinoma	11
Scirrhous carcinoma	5
Adenocarcinoma	1
Paget's disease	1

The retroperitoneal and/or aortic lymph glands were involved in only 11 cases, and in these the method of spread was explained on a lymphatic basis. It was explained on a vascular basis in 3 cases, and on peritoneal implantation in 1 case. In 3 cases it was uncertain.

METHOD	NUMBER OF CASES
Lymphatic	11
Vascular	3
Peritoneal implantation	1
Either vascular or lymphatic	2
Lymphatic or peritoneal	1

The determination of the method of spread is not easy. It was considered to be lymphatic when, for instance, in cases of breast carcinoma, the peritoneum was not involved and a chain of aortic and lumbar lymph nodes was enlarged and the tumor cells were seen in the lymphatic spaces of the ovary. When there were widespread metastases in most organs of the body and tumor cells were seen in blood vessels, then the method of spread was considered vascular. Surface implantation was considered the most likely route when there was peritoneal carcinomatosis with a surface lesion in the ovary. In many cases more than one method was obviously involved and when there was direct continuity between the primary and secondary, the method of spread was considered to be by direct extension.

Three cases deserve special mention. These came to autopsy 19, 14, and 12 years, respectively, after the primary was first noted. All three had undergone radical mastectomy soon after diagnosis was made and in the first two cases they were subjected to high voltage therapy as well. All were free of signs and symptoms until a few months before death, when the tumor suddenly reappeared in the form of multiple bony metastases producing spontaneous fractures, causing a rapidly downhill course and death. A diagnosis of primary ovarian carcinoma was made in only one of these.

B. Lung.—Of the two lung cases, one was a squamous-cell carcinoma and the other an adenocarcinoma. In both, only one ovary was invaded and neither the peritoneum nor the abdominal viscera were involved. In one the periaortic lymph nodes contained a few carcinoma cells. The spread in both was by the vascular or lymphatic route. We were struck by the relatively few cases of lung carcinoma that metastasized to the ovary, namely, 2 out of 157 cases (Table I).

C. Brain (Malignant Meningioma).—

This was an interesting case, as meningiomas only very rarely metastasize. Brain symptoms had been present for 19 years and a daignosis of meningioma of the brain was first made 7 years before death, at which time the tumor was removed. At autopsy there was a recurrence of the tumor at the site of operation and widespread secondary metastases. The ovaries contained a few tiny tumor nodules. The spread was by the blood stream.

Group II (Partial Topical Relationship to the Ovaries)

A. Stomach.—Eight cases of carinoma of the stomach metastasized to the ovaries. Of these, three were of the Krukenberg type and will be discussed briefly later. The method of spread in the eight cases is outlined as follows:

METHOD	NUMBER OF CASES
Lymphatic	3
Lymphatic or vascular	2
Lymphatic or peritoneal	2
Peritoneal implantation	1

B. Hepatic Flexure of the Colon.—In this case of adenocarcinoma, there was peritoneal carcinomatosis with ascites and extensive involvement of the ovaries. It was not possible to tell whether the secondary carcinoma of the ovary had spread by peritoneal implantation or through the lymphatics.

C. Liver.—The tumor was a cholangioma. Both ovaries were involved by pearly white discrete tumor nodules. The spread had taken place through the lymphatics or blood stream.

D. Gall Bladder.—This was a Krukenberg tumor to be discussed later.

E. Kidney.—This was a papillary carcinoma which involved both ovaries. The metastasis to the ovaries was probably through the lymphatics.

Krukenberg Tumors.—The 4 cases of Krukenberg tumor in this series fall in Group II, three having the primary in the stomach and one in the gall bladder.

The ages of the patients were 47, 38, 28, and 43 years. The tumors were bilateral in the first two, unilateral in the last two; in one of the latter the left tube and ovary had been removed many years previously for a different cause The peritoneum was involved in only 2 cases but there was ascites in all. The retroperitoneal lymph nodes were involved in all and the liver in two cases.

The clinical symptoms were epigastric in all, the pelvic symptoms not being prominent. In one case the stomach tumor was in the form of diffuse thickening of the wall and, in spite of all tests, could not be detected until autopsy. The tumor in one of the cases was extensive and located at the cardiac end and along the lesser curvature and involved the muscularis and serosa. The diagnosis was made on a biopsy from the axillary lymph gland. In the third gastric case, there was a perforated malignant ulcer on the anterior wall of the stomach after 4 years of epigastric distress.

The microscopic picture in the primary gastric carcinomas was that of a medullary carcinoma in one and a scirrhous carcinoma in the other 2 cases, and "signet cells" were present in all. In the gall bladder the picture was that of a colloid carcinoma.

In all four cases the ovaries showed the usual gross and microscopic features of Krukenberg tumors.

The method of spread in the case of the gall bladder and one of the stomach cases was through the lymphatics. In the other stomach cases it could not be ascertained whether the spread was through the lymphatics, blood vessels, or along the peritoneum.

Group III (Close Topical Relationship to the Ovaries)

A. Cervix Uteri.—All authors agree that carcinoma of the cervix very rarely metastasizes to the ovaries, and certainly much less frequently than carcinoma of the fundus. In this series there were 13 cases but in only 3 cases could the secondary carcinoma in the ovaries be definitely considered metastatic. In the other 10 cases the cervical carcinoma was so extensive that it formed a big pelvic mass involving all the pelvic organs, including the ovaries, and the spread was probably by direct extension. During the same period, 148 cases of carcinoma of the cervix came to autopsy, making the incidence of metastasis from the cervix 0.2 per cent. The moral from this is that the surgeon may preserve the ovaries in a young woman with carcinoma of the cervix.

The metastatic cases appear to have spread through the lymphatics. Of the 13 cases one was an adenocarcinoma and the others squamous celled.

B. Fundus Uteri.—In 1927, Novak[4] reported 174 cases of adenocarcinoma of the body of the uterus, in 7 of which there were metastases into the ovaries. He pointed out that the lymphatic route was the most important method of spread.

In our series there were 6 cases of ovarian involvement, out of which 3 were considered metastatic via the lymphatics and in the other 3 the tumor was too extensive to tell whether the invasion had taken place through the lymphatics, tubal lumen, or by direct extension. Probably more than one method of spread is responsible in a single case. During the same period 44 patients with carcinoma of the fundus came to autopsy.

C. Pelvic Part of the Large Intestines.—Of the 7 cases of carcinoma of the cecum, sigmoid, rectosigmoid, and rectum, 5 appeared to have involved the ovaries by direct extension. One case each of the cecum and rectum appears to have spread through the lymphatics.

D. Ovary.—In this series 3 cases were believed to be definitely secondary from the ovary. In one case the left ovary in a 22-year-old single girl was completely replaced by an anaplastic solid carcinoma, and the right ovary was secondarily invaded from serosal deposits, the ovary showing only a small tumor extending from the surface. In another case in a 44-year-old single woman a large papillary cystadenoma of one ovary metastasized into the wall of an otherwise benign serous cyst in the other ovary. In the third case a large papillary cystadenoma of the right ovary in a 43-year-old single woman showed deposits of tumor in lymphatic spaces in the left ovary.

E. Ureter.—This was a medullary carcinoma and appeared to have spread by direct extension and through the lymphatics.

Group IV (General)

This included 6 cases (lymphosarcoma 4, reticulum-cell sarcoma 1, and fibrosarcoma 1), which involved both ovaries diffusely and most of the organs of the body. The spread in these cases was obviously through the lymphatic or vascular channels.

In one case, the ovaries were involved by a large mass of adenocarcinoma in which the site of the primary tumor could not be determined.

Summary and Conclusions

1. In 10,287 autopsies on both sexes there was secondary ovarian tumor in 72 (0.7 per cent). Of these, 53 (73.6 per cent) could properly be called metastatic.

2. In the metastatic cases the primary tumor was most frequently found in the breast (34 per cent of cases), the stomach being the next most common site (15.2 per cent). Including malignant disease that had spread by direct extension as well, the cervix was the second most common site of primary disease.

3. Ovarian metastases occur in the same age group as the primary with one exception. Carcinoma of the breast metastasizes to the ovary more often before the menopause.

4. The ovarian tumors were bilateral in about two-thirds of the cases and both sides were equally involved in the remaining cases.

5. The ovaries were not enlarged in about half the cases, and therefore at operation involvement can easily be missed. As involvement of the ovaries is important in the prognosis of the primary disease, conclusions drawn from gross inspection of the ovaries is likely to be misleading.

6. The microscopic appearance in the large majority of cases was similar to that of the primary.

7. Pelvic symptoms were overshadowed by those of the primary in most of the cases and ovarian function was rarely disturbed.

8. In 62.5 per cent of the cases the peritoneum was not involved. Detectable ascites was present in 47.3 per cent.

9. In this series there were 4 Krukenberg tumors, 3 with a primary in the stomach and 1 in the gall bladder.

10. Carcinoma of the cervix involved the ovaries in 13 out of 148 cases. Of these, only 3 were metastatic (0.2 per cent). In a young woman with carcinoma of the cervix, the ovaries are rarely involved by metastases.

11. Carcinoma of the fundus extended to the ovaries in 13 per cent of the cases, but only half of these were metastatic.

12. The method of spread was lymphatic or vascular in the great majority of cases, direct extension and peritoneal implantation having occurred in only a few. In many cases more than one of the following methods took part in the process: (1) lymphatic, (2) vascular, (3) peritoneal implantation, (4) direct extension, and (5) through the tubal lumen.

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UNEXPECTED HYPERTENSION IN THE EARLY AND LATE PUERPERIUM

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IN 1934 Stout[1] reported on 102 patients in whom unexpected hypertension was recorded at the six weeks post partum examination. All of these patients during that particular pregnancy and labor showed normal blood pressure readings. Meyer[2] in 1938 and Meyer and Nadler[3] in 1941 reported, respectively, 23 and 51 cases of the same phenomenon. This report will deal with similar material with the addition of another group of patients, in whom the blood pressure elevations began after 48 hours post partum and before the six weeks examination. The illness which this group experienced has been designated "early unexpected puerperal hypertension." Its earliest appearance is at 48 hours post partum, so that there can be no chance of its being called pre-eclampsia. A concise definition may be somewhat as follows: Unexpected puerperal hypertension is an elevation of blood pressure in the parturient woman in whom previous pregnancies, if any, prenatal course, labor, and the first 48 hours post partum have not been accompanied by any readings of hypertensive character (130/90 and above). Any patient with a prior diastolic blood pressure of 90 or more was excluded.

Material

During the years 1940 to 1949, there were recorded on the "home delivery service" of the University of Maryland Hospital 5,612 Negro and 353 white registered patients. In this group there were 1 white and 164 Negro patients whose cases satisfied the definition given above. An accurate incidence cannot be given because many of the deliveries were repeat deliveries on the same patient, and several had two or more deliveries during this period of time on our "home service." We suspect that the true incidence will be close to Meyer's, 4.6 per cent. It certainly is not as high as Stout's incidence of 17.2 per cent. This wide range of incidence may be explained by the fact that any patient in our series, who, in any pregnancy of which we have a record, had a single elevation of blood pressure to 130/90, was excluded, as well as those whose blood pressure rose to abnormal levels immediately post partum (within 48 hours).

The average age level was somewhat above the clinic average, since in 88 per cent of deliveries the patients were over 20 years of age. One would expect a somewhat higher age level in an individual with hypertension (Fig. 1).

For the reason that few primigravidas are delivered on the "home service," only ten of these are in this group. From 1945 on, no primigravidas were accepted for home deliveries, and that lowers the incidence. The most frequent parity was one, and the number fell rather abruptly after parity four, as one would expect (Fig. 2).

Since most patients with hypertensive disease and/or pre-eclampsia will show blood pressure elevations during the last month of pregnancy, we included patients in whom only two or three prenatal blood pressure recordings were made. However, there were only 15 of these and the remaining 150 had four or more prenatal blood pressure recordings. The average number of recordings was six.

AGE

Fig. 1.

PARITY
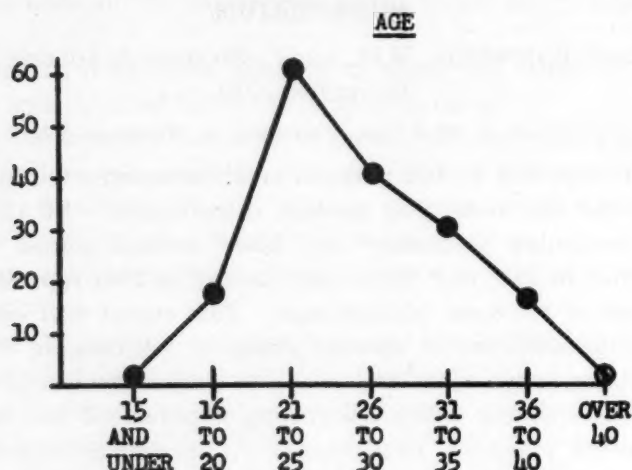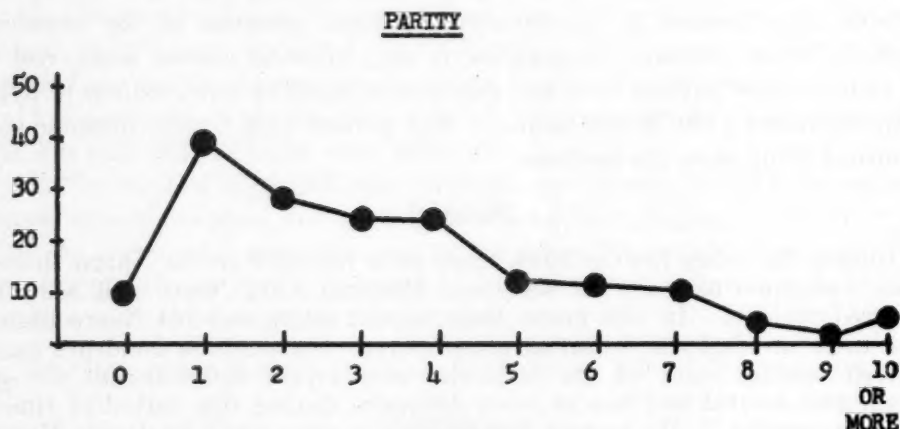
Fig. 2.

In Stout's and Meyer's series, there was no record of unexpected hypertension occurring before the six weeks examination or earlier in the puerperium. Of our 165 patients, 94 had elevations of blood pressure before the six weeks examination (Group "A") and 71 had their first recorded elevations at that time (Group "B"). Fifty per cent of the group with early unexpected hypertension (Group A) began their hyperpietic rise between the third and fifth postpartum days. In those who began having hypertension later, the number of primary elevations gradually decreased so that only 5 per cent of Group A had the initial rise between two and six weeks (Fig. 3). The blood pressure elevations following pregnancy lasted varying periods of time during the puerperium: in 2 patients only 2 days; in 29, 3 to 7 days; in 16, 8 to 14 days; and in 44, 2 to 6 weeks. Thirty per cent of those in whom a six weeks recording was made had normal blood pressures, while 70 per cent were still hypertensive (Table I).

TABLE I. DURATION OF ELEVATED BLOOD PRESSURE MAINTENANCE IN GROUP A

2 days	2
3- 7 days	29
8-14 days	16
2- 6 weeks	44
Total	91

In approximately 75 per cent of both groups the highest blood pressure rise at any time during the puerperium was of a less severe degree (130/90-159/99), and the remaining 25 per cent had elevations to 160/100 or more (Fig. 4).

Follow-Up

The follow-up results were most interesting, but quite contrary to those of Stout and Meyer. Stout reported 91 per cent of his patients as having only transient hypertension, and becoming normal by the end of one year, while 9 per cent had hypertension at the end of a year. Meyer and Nadler report that the phenomenon is self-limited and lasts from six to seventeen weeks. Our results show a high incidence of hypertension in follow-ups of one to ten years. These diverse results may be associated with the marked difference in the length of time of follow-up, but the incidence of hypertension in our series in which the follow-up was only one year was still excessive. Our results can be seen in Table II. Sixty-five per cent of the patients who were followed 1 to 10 years, had hypertension. Of those, two-thirds had mild hypertension (130/90-159/99), and the other one-third had the more severe grade (160/100 and over). Contact was lost with 37 patients, 2 of whom had died, one of carcinoma and the other from renal failure following an operation for nephrolithiasis.

TABLE II. FOLLOW-UP RESULTS

None	35
Died	2
Normal blood pressure	45
130/90-159/99	57
160/100 and over	26
Total	165

Of 128 patients followed, 83 or 65 per cent had hypertension.

Table III shows the varying length of follow-up. Most were from two to eight years, 16 were less than two years, and 10 were over eight years.

TABLE III. LENGTH OF FOLLOW-UP

None	37
0-1 year	16
2-4 years	65
5-8 years	37
Over 8 years	10
Total	165

Some correlation can be seen between the permanence of the hypertension and the height of the blood pressure in the early and late puerperium (Table IV). In Group A with the lower hypertension, about 50 per cent still have hypertension; in Group B with the lower hypertension, about 70 per cent still maintain elevated blood pressures; in Group A with the more severe elevations, puerperally, only 1 of 22 had normal blood pressure readings; and in Group B with the more severe hypertension, 60 per cent still have hypertension. This suggests that the patient who has an early rise of blood pressure, post partum,

has the greater chance of keeping her hypertension, but the number of patients is too small to make any definite conclusions. The higher blood pressure group in the puerperium also had a tendency to have a greater incidence of permanent hypertension and also higher permanent blood pressure.

TABLE IV. FOLLOW-UP BLOOD PRESSURE ACCORDING TO HEIGHT OF BLOOD PRESSURE POST PARTUM

	NORMAL	130-159	160 & OVER	NO RECORD
Group A 130-159	24	20	6	19
Group B 130-159	15	20	7	13
Group A 160 and over	1	11	10	3
Group B 160 and over	5	6	3	2

Those patients in Group A who still had hypertension at the six weeks examination were also analyzed (Table V). Their follow-up blood pressure recordings showed nothing unusual, except a tendency to have a somewhat higher rate of permanent hypertension.

TABLE V. GROUP A. FOLLOW-UP ACCORDING TO SIX WEEKS BLOOD PRESSURE

6 WEEKS BLOOD PRESSURE	NORMAL	130-159	160 AND OVER	NO RECORD
Normal	9	7	2	2
130-159	7	13	4	9
160 or more	1	2	4	3

Group A was also analyzed from the point of view of the length of elevation (Table VI). Two patients had elevations of only two days, and one of them has hypertension now. In the group whose elevation lasted 3 to 7 days, about 50 per cent are now normal. In those in whom it lasted 1 to 2 weeks, only 1 of 13 has a normal blood pressure and in the longer-lasting group, 10 of 31 have normal blood pressures. The length of elevation, originally, does not seem necessarily to be a factor in the long-range view of hypertension.

TABLE VI. FOLLOW-UP ACCORDING TO LENGTH OF ELEVATION. GROUP A

LENGTH OF ELEVATION	NORMAL	130-159	160 AND OVER	NO RECORD
2 days	1	0	1	0
3-7 days	12	9	2	6
8-14 days	1	9	3	3
2-6 weeks	10	13	8	13

Does the length of follow-up influence the results concerning permanent hypertension? These results can be seen in Table VII. There seems to be a consistently higher rate as length of follow-up increases. Obviously, these patients are also older and hypertensive rates increase with age.

TABLE VII. HYPERTENSION BASED ON LENGTH OF FOLLOW-UP

	NORMAL	130-159	160 AND OVER	
1 year	8	5	3	50%
2, 3, and 4 years	26	25	12	60%
5, 6, and 7 years	8	19	6	76%
8 years and over	3	7	3	77%

Seventy-five of these 165 patients were followed through one or more pregnancies subsequent to the onset of this phenomenon. Only four patients in both groups had evidence of hypertensive disease during their subsequent pregnancies. However, 24 of 30 in Group A and 33 of 42 in Group B again had hypertension during the puerperium of subsequent pregnancies. The 4 patients who did show hypertension during pregnancy had the elevation late and on two occasions it was associated with albuminuria. This observation emphasizes the difficulty of recognizing hypertensive disease during pregnancy. If the past history of these patients were not known, 71 of 75 would be classified as normal patients during pregnancy and the remaining 4, who did show hypertension, might very well have been classified as pre-eclamptic. Blood pressure drops normally during normal pregnancy and this also holds true for the chronic hypertensive individual.
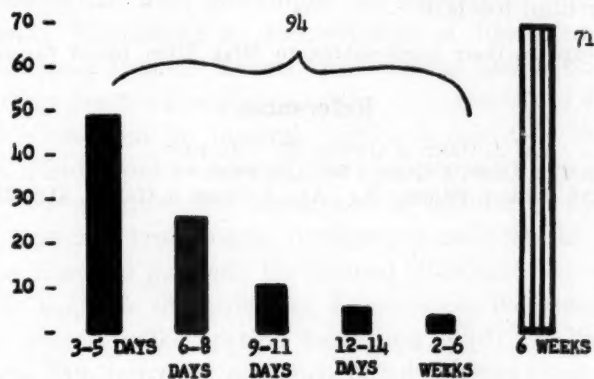
Fig. 3.—Time of onset of elevated blood pressure post partum.
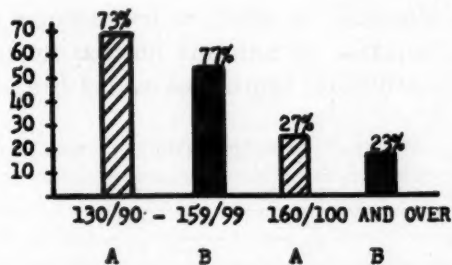
Fig. 4.—Height of blood pressure post partum. Group A, Immediate postpartum hypertension. Group B, Hypertension at six weeks examination only.

Comment

Unexpected puerperal hypertension can occur both early and late in the puerperium, and it is not uncommon. It is essentially limited to the Negro race; however, it can occur in the white race. Previous reports on this subject indicated that it is largely a transitory phenomenon and needs no consistent follow-up. We found, however, that there was permanent hypertension in 65 per cent of the cases. This study also emphasizes the importance of past history in the final analysis of all hypertensive states during pregnancy to arrive at the correct diagnosis of the toxemia that the individual is experiencing. Because many of these hypertensive rises occur fairly early in the puerperium, we should not refrain from recording blood pressures in post-

partum patients after 48 hours; but the blood pressure should be taken repeatedly as long as possible in order that these rises may be noted and the patient followed for a much longer period of time.

Conclusions

1. Unexpected puerperal hypertension should be considered because of its remote hypertensive effects.

2. The study of these patients emphasizes the difficulty of making the diagnosis of hypertensive disease during pregnancy.

3. In the postpartum period, the recording of blood pressure should be more frequent and over a longer period of time, so that remote permanent hypertension can be suspected and adequate medical therapy instituted immediately, rather than too late.

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NATURAL CHILDBIRTH IN A GENERAL HOSPITAL

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WHAT has come to be called natural childbirth is not new. However, a greater number of individuals are now enjoying childbirth as a normal and natural or physiological process. There has been an increasing awareness of the importance of the total individual, his personality and emotions, in all fields of medicine. Stimulated by the writings of Read,[1] and more recently those of Goodrich and Thoms,[2] Thoms,[3] and Thoms and Roth,[4] this same consideration is finding greater acceptance in the management of childbirth. Since the adoption of a program for natural childbirth might be thought to involve special facilities, funds, and personnel, the experience at The Genesee Hospital is of interest. Our program has functioned satisfactorily despite the lack of such factors, as would be true in any average general hospital.

The Genesee Hospital program for natural childbirth is now approximately one year old. To evaluate this program, a representative sampling is presented which covers a seven months' period beginning Sept. 17, 1949. During this period there were 749 deliveries of which 661 deliveries were performed by 32 different private physicians and 88 by the house staff. Two hundred fifteen deliveries, or 28.8 per cent of all deliveries, are reported as examples of natural childbirth. These are summarized in Table I. The sole criterion for selection of these patients was antepartum training or intrapartum support which is characteristic of the method known as natural childbirth.

TABLE I. DISTRIBUTION OF PATIENTS

	TOTAL	PRIVATE	STAFF	SECTIONS
All cases	749	661	88	21
Natural childbirth	215	157	58	0

The program has been informal to the extent that participation is voluntary for both the physician and the patient. Labels such as "Read patient" were avoided. The efforts have been directed toward the establishment of a sound patient-physician relationship and regard for the patient as an individual with her own total personality. Having avoided any attempt to "sell" the program, it has functioned without friction. This is now supported by the increasing number of physicians and patients who are participating in the program as contrasted to those participating at its inception.

The antepartum training has been variable. Some of the patients had no indoctrination prior to the onset of labor. Others had minimal training through reading of various books and talks with friends and relatives. At the start of the program, two of the physicians indoctrinated their patients at the time of

the prenatal office visits. A program of class instruction for expectant mothers was begun in February, 1950. This latter program has proved the most successful method of training. Four classes are repeated at monthly intervals to cover the topics of pregnancy, exercises, care and behavior of the newborn, and labor.

The class program has been administered by the resident house staff and the nursing staff. The instruction has been practical and factual. No promises are made. The attempt is to orient the patient generally relative to the total experience of pregnancy and subsequent parenthood. Questions are encouraged while consultation with the physician concerned is urged where the problems are peculiar to the individual. The exercises are presented so that they may be incorporated in the patient's usual routine. They do not become something requiring special effort. The exercises are practical in that their object is to improve posture, to condition the muscles and joints which undergo stress during labor, and to teach the practical techniques of relaxing that increase comfort during labor. Since the program began there has been an increase of over 500 per cent in both the number of patients attending the classes and the number of physicians who refer their patients.

Supplemented by consultations with the individual physicians concerned, optimal training has been obtained with this class program. The patients enjoy the experience of group training with its exchange of information. The classes are spirited and pleasant for both the students and the instructors. The private physicians find the classes valuable not only for the time saved but especially since they are assured that all of their patients will receive the same basic information. Individual office instruction is not only time consuming, but it is impossible to give uniform instruction whereas class instruction is controlled and complemented by individual consultation. Guided supplementary reading is helpful. *Understanding Natural Childbirth* by Thoms and Roth[4] has been written especially for the patient to supply the same sort of information which is given in class instruction. However, the patient who "does it on her own" is rarely successful. Cooperation between the physician and patient is essential.

Individualization is stressed in both the prenatal training and the support during labor. The patient is impressed with the idea that each labor and pregnant woman is different and has different needs. The actions and uses of medications and anesthesia are explained, as are the other methods of support utilized to meet the needs of the individual patient for comfort during labor. Consequently, no patient feels that she is part of an "experiment." No patient is led to believe that she has failed when her experience does not coincide with the ideal accounts of childbirth which have been so glowingly presented in some writings. Each patient is satisfied even if she might not be classified as "successful." The avoidance of routines and labels is paramount in order to obtain satisfied patients.

The meaning of support during labor has been described previously.[3] The basis of support is a pleasant atmosphere arising from understanding and respect of the participants for each other. This is evident in the reactions of those participating either actively or passively in the experience of childbirth more through obligation or duty than through genuine interest. There is a significant turnover in house staff, nursing staff, student nurses and the fourth-year medical students serving as externs for brief periods. This change of personnel as well as the number of personnel available in a general hospital limit coverage of the service at all times by those who might be especially interested in natural childbirth. The support, therefore, is not always ideal.

Despite these obvious obstacles, the program has been satisfactory. One or two individuals can do much to perpetuate the program. When possible

results are demonstrated, interest is aroused and others seek to learn more about the program. Some of our best results have come about from just such interest on the part of medical students and student nurses. Similarly, it is obvious that in several instances results would have been better had the attendant been more sympathetic and understanding. The patients are quick to sense this difference in support. In discussing their experiences, patients not only expect proper scientific obstetrical care but they also appreciate skillful practice of the art of medicine. Even as patients encourage one another during labor, they urge their expectant friends toward natural childbirth.

Further data concerning the seven months' experience are given in Tables II, III, IV, and V. Although this group of patients is too small to be significant statistically, it is clear that the cross section selected does not vary from the experience to be expected in any general hospital. All of the hemorrhages reported were judged to be due to uterine inertia. There was no frank eclampsia. There was no maternal mortality. All complications responded to usual methods of conservative therapy.

TABLE II. PARITY OF PATIENTS

	TOTAL	PRIVATE	STAFF
Primiparas	75	61	14
Multiparas	140	96	44

TABLE III. DISTRIBUTION OF PRIVATE PATIENTS

PHYSICIAN	A	B	C	D	E	F
Number of patients	84	58	10	2	2	1

TABLE IV. COMPLICATIONS

	NUMBER	PER CENT
Premature birth	5	2.18
Breech presentation	5	2.18
Twin birth	4	1.86
Neonatal death	1	0.46
Stillbirth	1	0.46
Maternal morbidity	9	4.18
Maternal one-day fever	5	2.18
Hemorrhage due to uterine inertia	6	2.64
Pre-eclamptic toxemia	4	1.86

TABLE V. INDICATIONS FOR FORCEPS DELIVERY

Low Forceps.—	
Prolonged second stage	19
Elective	17
Contracted outlet	5
Fetal distress	3
Prophylactic (premature)	2
Persistent occiput posterior	2
Transverse position	1
Aftercoming head	1
Midforceps.—	
Cephalopelvic disproportion	3
Transverse arrest	2

There were 57 operative deliveries. This includes one breech extraction and one version extraction for transverse arrest. The elective forceps were for patients who had lost control and were either too tense or uncooperative to effect

spontaneous delivery. They represent the disadvantages of the personnel problems previously discussed where support was neither adequate nor available under the circumstances to be met at times in a general hospital. The other patients who had operative deliveries benefited from the support given and enjoyed more comfortable labors. Likewise, the patient with a question of cephalopelvic disproportion undergoing a trial labor prior to cesarean section will benefit from a more comfortable labor through the techniques of support. The transition to operative delivery is made more smoothly with the patient who has been trained and given support.

One patient deserves added comment because of the unusual aspects of her uterine inertia. This patient, a para i, gravida ii, at term, had a normal spontaneous delivery without medication or anesthesia after a total labor of three and one-half hours. The intact placenta delivered spontaneously. The immediate blood loss was less than 100 c.c. During the second postpartum hour, uterine inertia developed with resultant hemorrhage. The usual oxytocic drugs and massage failed and it was necessary to pack the uterus and treat secondary shock. With these measures the hemorrhage was controlled after a period of several hours. The inertia of this uterus was similar to that seen with the Couvelaire uterus. The necessity for hysterectomy was avoided only through the extended effort of those in attendance. This instance of delayed uterine inertia indicates that good obstetrical and nursing care is as important in natural childbirth as in "routinized" obstetrics.

Anesthesia is given by the Department of Anesthesiology. All types of anesthesia have been used except caudal anesthesia. There is no particular reason for this exception since it was used during the same period for patients not considered to be experiencing natural childbirth. The choice of anesthesia is made by the obstetrician and the anesthesiologist for each individual patient according to the needs of the patient and the obstetrical situation.

Local anesthesia, either as local infiltration or pudendal block, has proved to be very useful. It is not used routinely but is adaptable to many patients. The patient must understand that it alters sensation but does not eliminate deep pressure sensation. To avoid loss of potency, a fresh 1 per cent solution is made for each delivery by diluting ampuls of 50 per cent procaine with Cobefrin. The technique of administration is simple.[5] The anesthesia is satisfactory for the repairs which are indicated. The relaxation of the perineal floor facilitates both spontaneous and operative delivery and is equal to the relaxation obtained with spinal anesthesia. Local anesthesia also has a general analgesic effect which aids in its efficiency.[6]

The results of this program may be evaluated in several ways. First, there is the obvious satisfaction of the patients. They appreciate the care given them as support during labor. This applies not only to their obstetrician but also to the hospital and its staff. This is reflected in the happy spirit and pleasant atmosphere which result both directly and indirectly. Even those patients and physicians who do not participate in the program are aware of this change.

It is the impression of the physicians practicing natural childbirth that the duration of labor is less. Certainly there is less confusion between false and true labor on the part of both the obstetrician and the patient. The physician with the largest number of patients in this group notes the shorter duration of labor and has commented on the fact that patients come to the hospital at a later stage of labor. This physician finds that he is now spending less time with his patients. His patients previously came to the hospital early in labor and had longer labors. He was more restricted and spent more time going in and out of the hospital for each labor. Most patients now deliver within two or three hours after admission. This is the answer to the criticism that natural

childbirth is more time consuming. All of the physicians report that their patients know what is happening and when to do something. There are fewer phone calls and visits for false labor and other functional symptoms.

The babies are in better condition at birth. They frequently begin to cry as the head is born. Their color, reactions, and respirations are better. This is in marked contrast to previous experience when routine medication and anesthesia were used. Under such a regime, a majority of the babies were born in a condition that should be classified as the first stage of asphyxia.[7] This was not appreciated since it was so common. The baby had to be flaccid before he would be regarded as showing any degree of asphyxia. An awareness of the significance of asphyxia as a cause of central nervous system damage indicates the value of natural childbirth which avoids depression of the baby at birth and in the immediate neonatal period.

There is also the impression that blood loss during the third stage is less. Although uterine inertia may still occur, the average blood loss is less and frequently is so small as to be negligible. The incidence of greater blood loss and damage to maternal tissues with increased medication, anesthesia, and operative incidence is stated in our textbooks. The physician is impressed by the frequent spontaneous delivery of the placenta. Needless to say, the patient prefers this to vigorous attempts at manual expression of the placenta.

No serious attempt was made to interview these patients since no qualified person was available to interview and evaluate the answers. Certain impressions remain from informal discussions of childbirth with these patients. There is an evident pride in individual accomplishment and satisfaction in the knowledge that they were responsible for the birth of their babies. Their efforts were guided and usefully employed so that labor did not leave them exhausted from wasted effort during the first stage. They recover quickly from the effects of childbirth and they are less fatigued. There are obvious psychological implications in natural childbirth, but any profound evaluation will have to await the results of such studies being carried out elsewhere.

Since the program is most concerned with the discomfort of childbirth, this must be evaluated. There is no reliable subjective indication of discomfort which can be applied as a standard. This is recognized in the effort of the program of training and support to maintain each individual's threshold for discomfort at or near a basal level. Objective measurements are similarly restricted but a relative evaluation may be obtained by indirect, albeit arbitrary, methods.

To consider as many factors as possible, the following system was employed. The discomfort of each patient was expressed in terms of units. The number of units of discomfort is represented by the number of units of medication or anesthesia necessary to cancel out the discomfort. Each 100 mg. dose of Demerol, Seconal, or Nembutal is rated as one unit. Intermittent inhalation anesthesia and local anesthesia for delivery are each rated as the equivalent of one unit. Continuous inhalation anesthesia and spinal anesthesia are each rated as the equivalent of two units. The discomfort experienced by each patient can be classified by the sum of the units of medication and anesthesia. The over-all distribution is tabulated in Table VI.

TABLE VI. EXTENT OF DISCOMFORT IN CHILDBIRTH

Units*	0	1	2	3	4	5	6
All cases	17	54	74	51	12	5	2
Primiparas	3	16	20	23	8	3	2
Multiparas	14	38	54	28	4	2	0

*For definition of Units, see text.

When this distribution is expressed as a curve (Fig. 1), an interesting result is obtained. The similarity of this curve to the familiar general distribution curve for other personality traits is apparent. This study indicates that discomfort during labor is a function of the individual patient's total personality. The importance of individualization of the management of the obstetric patient, as in natural childbirth, is obvious. The validity of routine medication and anesthesia, or any other routine, is denied. The satisfactory understanding of natural childbirth becomes directly dependent upon an appreciation of the need for individualization since the discomfort of childbirth is a function of the individual's total personality. Helene Deutsch[8] indicates the basic fears of death during childbirth and birth of a monster. Training and support will not eliminate these fears, but the effects may be mitigated through the elimination of other fears. Individualized training and support are the best means of maintaining each patient's threshold for discomfort at a basal level. The result is pleasant for both the physician and the patient.
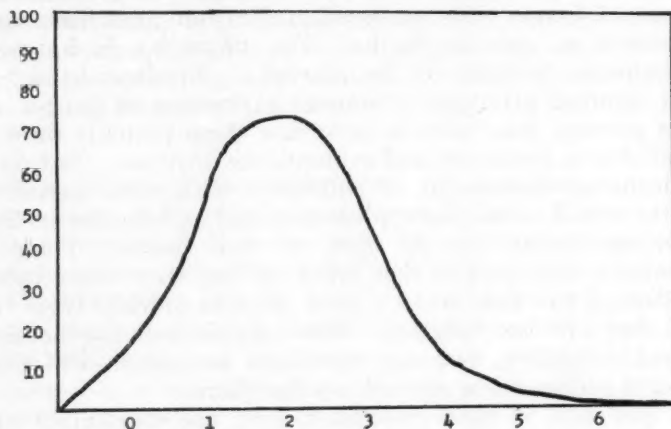
Fig. 1.

In conclusion, natural childbirth is practical in a general hospital. Despite obvious difficulties and obstacles, satisfactory results may be obtained. No special measures were necessary. The acceptance of natural childbirth is becoming more widespread because of its practical nature and a better understanding of its significance when viewed in proper perspective.

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STUDY OF POST-SPINAL ANESTHESIA HEADACHES

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DUE to the increased use of spinal anesthesia and the publicity that it has received in papers, magazines, and journals, the lay person, and especially the pregnant woman, has exhibited great concern and fear. Occasionally the relatively infrequent disadvantages are voiced the loudest. Almost every physician, and particularly the obstetrician, has been confronted by the patient who requests not to be given a spinal because she fears the postspinal headache. Due to this situation and also because we were impressed with the relative frequency of headaches among the postpartum patients, our interest was aroused in a search for a means of prevention, or a more rapid method of cure than is available at the present time.

Various complications of spinal anesthesia are mentioned in the literature, such as headache, decrease in blood pressure, uterine atony, nausea and vomiting, intrathecal infections, and neurological complications. Headache is usually mentioned as the most frequent obstetrical complication. The incidence of headache following spinal anesthesia for vaginal delivery as reported in the literature varies from 0 to 19.5 per cent.[1-7]

There is general agreement that most spinal headaches occur within the first five, and usually within the first two or three, days following delivery. The headaches may occur in the frontal, temporal, or occipital areas. The duration of the headache is usually under two days, and only on rare occasions is the discomfort so severe that it does not respond to codeine, or that the patient is required to remain flat in bed for longer than one or two days beyond the usual time.

There are many theories ascribed to the etiology of postspinal headaches such as season of the year, increased concentration of pituitary and other hormones, foreign body reaction, fatigue, and allergic reactions. However, the two most recognized theories are that the headache is due to the hypodynamics of the cerebrospinal fluid or to the pooling of blood in the splanchnic vessels and in the lower extremities. Wolff[8] describes the postspinal headaches as being due to the leakage of cerebrospinal fluid through the dural hole in the lumbar sac. He has found that the drainage of approximately 20 c.c. of cerebrospinal fluid will produce headache in a normal erect subject. Wolff believes that this type of headache is due to the decrease of the cerebrospinal fluid pressure which allows the brain to settle on its pain-sensitive intracranial structures. Weintraub[5] believes that spinal headaches following vaginal delivery are due to the pooling of blood in the splanchnic vessels induced by the sudden release of

intra-abdominal pressure occurring post partum, which is further augmented
by the vasomotor paralysis due to the action of the spinal anesthesia on the
splanchnic nerves.

Material and Methods

Three hundred eight-eight pregnant women admitted to Cleveland City
Hospital's obstetrical service were given a low (saddle block) spinal anesthesia
for vaginal delivery. These three hundred eighty-eight consecutive cases were
divided according to race, age, and parity, as shown in Table I.

TABLE I

NO. OF PATIENTS		
A. Race.—		
White	112	
Negro	276	
		Total 388
B. Age.—		
Under 20 years	67	
20-24 years	166	
25-29 years	95	
30 and over	60	
		Total 388
C. Parity.—		
Para i (First pregnancy to be delivered)	88	
Para ii-iv	257	
Para v and over	43	
		Total 388

When the cervix was fully dilated and the fetal head had descended to a
plus one or two station the patient was turned on her side with her head and
knees in as close approximation as possible. A No. 20 spinal needle was inserted
at the third lumbar interspace and as little fluid as possible was lost. A 1:1
mixture of Pontocaine (5 mg.) and 10 per cent dextrose was then slowly in-
serted into the subdural space. The head was elevated to a 30 to 40 degree
angle five to ten seconds later by means of a wooden back support. The level
of anesthesia was checked closely and never rose above the umbilicus.

Following delivery the patient was observed for one hour and then trans-
ferred to the postpartum floor. Orders were routine except that codeine and
salicylates were eliminated. Patients were kept flat in bed for 48 hours follow-
ing delivery. Daily rounds were made on all patients by the ward doctor and
nurse. At no time was mention of headache made. If the patient volunteered
the complaint of headache, she was then questioned as to when it first occurred,
the area affected, and the severity.

When the patient reached the postpartum floor she was started immediately
on one of five different courses of therapy in an attempt to find the best pro-
cedure to prevent or minimize postspinal headache. The types of therapy ad-
ministered were: (1) abdominal binder of 12 inch stockinette was stretched
tightly over a folded bath towel placed on the abdomen, (2) Prostigmine hydro-
chloride 15 mg. orally twice a day, (3) elixir of Benadryl one dram (15 mg.)
orally three times a day, (4) Benadryl 50 mg. orally twice a day, and (5) nico-
tinic acid, 50 mg., orally twice a day. In addition a control series was studied
in which no medication except Ergotrate was given.

Results

Table II suggests that the race of the patient does not influence the inci-
dence of headaches. Fourteen (12 per cent) of the white patients and forty
(14 per cent) of the 276 Negro patients developed headaches.

TABLE II

RACE	NO. CASES	NO. HEADACHES	PER CENT OF HEADACHES
White	112	14	12
Negro	276	40	14

The study of the frequency of headache following spinal anesthesia reveals that age and parity deserve some consideration. In Tables III and IV it can be noted that of 67 patients under 20 years of age, only 5 (7 per cent) suffered headache and only 7 (8 per cent) of the 88 patients delivered of their first child developed a headache. On the other hand, 12 (20 per cent) of the 60 patients over 30 years of age and 12 (28 per cent) of the patients para v or more developed typical postspinal headaches. Table V lists the frequency of headaches following one of the five courses of therapy listed. Comparison with the control series demonstrates that the abdominal binder was the best type of therapy used to decrease postspinal headaches. Prostigmine HCl did not appear to have any significant influence. However, Benadryl and nicotinic acid exhibited a detrimental effect doubling the frequency of headache. An attempt will be made later to show reasons for these responses.

TABLE III

AGE (YEARS)	NO. CASES	NO. HEADACHES	PER CENT OF HEADACHES
Under 20	67	5	7
20-24	166	22	13
25-29	95	15	15
30 and over	60	12	20

TABLE IV

PARITY	NO. CASES	NO. HEADACHES	PER CENT OF HEADACHES
Para i	88	7	8
Para ii-iv	257	35	14
Para v and over	43	12	28

TABLE V

	NO. PATIENTS	NO. HEADACHES	PER CENT OF HEADACHES
Control	109	10	9.1
Abdominal binder	61	4	6.5
Prostigmine HCl	83	10	12.0
Benadryl No. 1	35	6	17.0
Benadryl No. 2	30	8	26.6
Nicotinic acid	70	16	22.9

Comment

Why do some people develop postspinal headaches, and others do not when exactly the same technique, amount, and type of anesthetic drug is used? Some authors[6, 9, 10] claim headache is caused by a toxic reaction to various anesthetic drugs. Parmeley and Adriani[1] found no such reaction to the Nupercaine used by them. The size of the needle has caused much discussion. Some investigators[11, 12] place much emphasis on the use of the small needle, others[3, 13] do not feel that the larger (No. 20) needle increases the incidence of headache. Schmitz and Baba[6] agree with the latter but state that as little fluid as possible

should be lost. Adler[14] reports that headache occurs (13 per cent) after a simple diagnostic tap. Headache was noted to occur less frequently when early ambulation was used,[6] and also following cesarean section and routine abdominal surgery.[4, 5, 6] Various drugs, such as ephedrine, Benzedrine, Gynergen, aspirin, and codeine, have been tested and proved of little value.[5]

Much has been written concerning the etiology of postspinal headaches.[5, 8] We would like to add our theory based on our response to abdominal compression. A review of anatomy shows that the dural sac which envelops the spinal cord and fluid is surrounded by a group of veins (medulla spinals and internal vertebrals) which communicate with the inferior vena cava via the lumbar and the intervertebral veins. We suggest that abdominal compression causes an increased pressure within the vena cava which is transferred back through the lumbar and intervertebral veins to the plexus of veins surrounding the dural sac. Because the dural sac and the veins surrounding it are enclosed in a bony case, this increased venous pressure can be equalized only by a decrease in the space occupied by the spinal fluid. This equalization of pressure causes a rise in the cerebrospinal fluid pressure lifting the pain-sensitive structures of the brain from the cranial bed, thereby relieving the headache. This course of events is similar to the physiological explanation ascribed to the Queckenstedt test. Further support of this idea is offered clinically by (1) the sudden increase in cerebrospinal fluid pressure and (2) the sudden relief of headache following abdominal compression. In addition, the increase in frequency of headaches with age, parity, and vasodilator drugs tends to coincide with our suggested theory of etiology for postspinal headaches.

We feel that there is no procedure which we have tried which will eliminate postspinal headaches, but that abdominal binder is the best means of prevention or cure available at this time. It is felt that abdominal compression is especially indicated in elderly primiparous and grand multiparous patients whose abdominal muscles are markedly relaxed and also in those patients whose cerebrospinal fluid pressure is low or border line when the initial tap is performed.

Summary and Conclusions

1. In 388 consecutive cases of spinal anesthesia, 54 postspinal headaches were reported.

2. The postspinal headaches occurred on the second or third postpartum day or when the patient first assumed the erect position.

3. The race of the patient did not influence the incidence of postspinal headaches.

4. The frequency of postspinal headaches increases as the age of the patient increases. A marked rise in postspinal headaches in patients over 30 years of age was noted.

5. As parity increases, the frequency of postspinal headache increases proportionately.

6. In our hands, abdominal binder is the most satisfactory method of treating postspinal headaches.

7. Prostigmine, Benadryl and nicotinic acid proved of no value as preventives or cures for postspinal headache. The latter two showed a suggestive increase in the frequency of headaches.

8. Because headaches appeared more frequently with an increase in age and parity, a decrease in muscle and vascular tone is suggested as a contributory cause of postspinal headaches.

9. A theory concerning the etiology of postspinal headaches including the hypodynamics of the cerebrospinal fluid, venous pooling of blood, and muscle relaxation is suggested.

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2105 ADELBERT ROAD

CANCER OF THE CERVIX

A Realistic Program of Cancer Control for the General Practitioner

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PREVENTION, at the present time, rather than early diagnosis of carcinoma of the cervix should be the primary goal of the general practitioner in a program of cancer control. Early diagnosis of carcinoma of the cervix presents several insurmountable economic and diagnostic problems to the average examining physician. The diagnosis of early carcinoma of the cervix *cannot* be made without the help of cervical biopsies and/or Papanicolaou vaginal smears. These tests are expensive, and if widely used there would be a lack of trained personnel to interpret them. Since it has been shown that better than 50 per cent of those patients with early carcinoma will be alive five years from now as against less than 10 per cent of those with advanced carcinoma,[1] the physician knows the importance of early diagnosis of carcinoma of the cervix. It is a sad reflection on modern medicine that we continue to find 60 per cent of women with carcinoma of the cervix in an advanced state when treatment is begun.[1] The chance of cure in carcinoma of the cervix decreases 15 to 20 per cent for each month in delay from the onset of abnormal bleeding to the beginning of treatment, with the average time from the onset of symptoms to the beginning of treatment being 7.5 months.[2, 3]

Unfortunately, there are no early symptoms or signs of carcinoma of the cervix except leucorrhea. Leucorrhea (possibly the most common gynecologic symptom seen in the practice of medicine) often means a diseased cervix and demands a scrupulous examination of that organ.[4] This leucorrhea is always caused by the proliferative mass present. Meigs[5] believes that *bleeding between periods without any apparent reason* is an important symptom of carcinoma of the cervix. Postcoital and post douche bleeding, as well as the presence of blood on underwear, nightgown, or bedclothes, should make one particularly suspicious of cancer. This bleeding is first noted when the tumor begins to outgrow its blood supply, causing an ulcerative necrotic area in the rapidly growing tumor mass. When pain, intermittent bleeding, and a watery, foul-smelling discharge are encountered, it may be concluded in most cases that an advanced tumor is present. Clinical experience with cancer of the cervix caused the late C. Jeff Miller to state that "the symptoms of cancer of the cervix are the symptoms of death."[6]

The Schiller iodine test, which is so frequently mentioned as an aid to diagnosis of cancer, is of real value in helping one to decide where to biopsy a suspicious looking cervix. It must be emphasized, however, that this test is in itself not accurate in detecting carcinoma of the cervix since it is 90 to

95 per cent positive in benign cervical lesions.[7] Normally, the squamous epithelium of the cervix and vagina turns a deep brown on exposure to iodine because of its high glycogen content. Since carcinoma cells are glycolytic, they fail to take up this iodine stain. However, it has been found that the normal endocervical epithelium and areas of cervical leucoplakia also fail to take up the stain.

It is impossible to differentiate grossly between a chronically infected cervix and a cervix with early carcinoma.[8, 9, 10] Hinsellman[11] erred 50 per cent in his initial diagnosis of cancer in 450 cases of leucoplakia in 18,000 cervices observed through a colposcope at a magnification of 10×. Microscopic examination further showed that only 2 per cent of these cases of cervical leucoplakia were carcinomatous.

Since it is impossible to detect an early cervical carcinoma on gross appearance, the various diagnostic cancer clinics are committed to doing routine biopsies on all diseased cervices. The Papanicolaou vaginal smear is being used with ever-increasing efficiency to complement the cervical biopsy in making an early diagnosis of cervical cancer. It might seem ideal to subject every woman examined by the general practitioner to a cervical biopsy and/or Papanicolaou vaginal smear. From a practical and economic viewpoint, however, these laboratory procedures are beyond the bounds of general practice for two reasons:

1. A cervical biopsy and vaginal smear are costly and far exceed the cost of an office visit in most cases.

2. There are only a handful of really competent vaginal cytologists in this country and about 1,500 tissue pathologists. These persons could not possibly examine more than a fraction of the biopsy material with which their laboratories would be swamped.

Since it is impossible to make a diagnosis of early carcinoma of the cervix without expensive and time-consuming laboratory procedures, it is believed that prevention rather than the early diagnosis of carcinoma of the cervix should be the chief goal of the general practitioner in a program of cancer control. Electrocauterization of the cervix has been shown to be an extremely valuable prophylaxis against carcinoma of the cervix.[12-17] Huggins,[12] and Pemberton and Smith[18] failed to pick up a single case of carcinoma of the cervix in 4,393 diseased cervices which had been cauterized. These statistics are particularly impressive since Meigh[19] estimated that 2 to 3 per cent of all parous women over the age of 30 years ultimately die of uterine cancer, while Younge and co-workers[9] found a 4.4 per cent incidence of carcinoma in situ and invasive carcinoma of the cervix in 2,262 specimens examined microscopically.

Electrocauterization of the cervix will cure 85 per cent of patients with carcinoma in situ of the cervix when the disease is limited to the surface of the cervix.[9] Carcinoma in situ is now believed to represent the beginning of an eventually invasive cancer.[10] The patient's life is not jeopardized by the delay

if cauterization fails to cure the carcinoma in situ since it is believed that about 10 years are required for this type of carcinoma to become an invasive tumor.[10]

Pemberton and Smith[18] had not been able to find a single patient out of 669 with carcinoma in whom the cervix had been cauterized before the onset of the cancer. Review of 225 cases of carcinoma of the cervix observed during the years 1939 to 1949 at the Gynecology Tumor Clinic of the Ohio State University Hospital showed that:

1. Not one of the 225 women with carcinoma of the cervix had had the cervix cauterized before the onset of the cancer.

2. Five patients with carcinoma of the cervix had had the cervix cauterized before the diagnosis of cancer had been established by cervical biopsy. Three of these women had had the cauterization within two months of the positive biopsies for cancer. In all three of these cases, the cancerous growth was limited to the cervix at the time of the cervical biopsy. In the fourth and fifth cases, respectively, bleeding had persisted for nine months and leucorrhea for twelve months after cervical cauterization before a biopsy for cancer had been obtained. It was interesting to note that despite the tardy diagnosis of cancer in these two cases, there had been no extension of the cancerous growth to the pelvic wall at the time of the cervical biopsy.

About 85 to 95 per cent of women bearing children have cervicitis and erosions of varying degree.[12, 16] In fact, it is seldom that one finds a healthy cervix free from all evidence of inflammation even months after delivery. Cancer is more likely to develop when the chronic irritation of a local lesion is added to the still unknown constitutional factor responsible for cancer. W. J. Mayo has been quoted as saying that cancer has never been found where there is no chronic irritation, and Bloodgood said that cancer has never been found in healthy tissue.[20] Pemberton,[18] Huggins,[12] and Bland[13] believe the important etiological factor in carcinoma of the cervix to be the erosive irritative action of the secretions of the infected endocervical glands on the surface epithelium of the cervix. These infected endocervical glands extend deep into the cervical stroma. Since the endocervical infection is usually deep seated, the local application of antiseptics such as silver nitrate, iodine, Merthiolate, etc., is not only ineffective but futile.[4] It was Dickinson[21] who in 1921 popularized the use of the electrocautery to burn out and destroy the infected endocervical glands present in chronic cervical infection.

If one accepts the general principles outlined in the foregoing discussion, it follows that all chronically infected cervices should be treated by electro-cauterization as a prophylaxis against carcinoma of the cervix. This usually can be done effectively in the physician's office. The cervix should be carefully examined 6 to 8 weeks after the cauterization and slight unhealed erosions recauterized at that time. All those erosions which have not healed well should be considered as being carcinomatous until proved otherwise and, if possible, the patient should be referred to a Cancer Diagnostic Clinic or a gynecologist for further study. At that time, the unhealed diseased cervix should be biopsied at 6 and 12 o'clock at the junction of the erosion and the

normal-appearing squamous epithelium of the cervix. Other sites are biopsied in accordance with information gained from carefully performed and carefully interpreted Schiller tests. The Papanicolaou vaginal smear should be used to complement the cervical biopsy, but it is also extremely important to remember that this test should not be used to replace the cervical biopsy. Using this test alone, even the competent vaginal cytologist obtains a 10 per cent false negative result for carcinoma of the cervix[22] and more than 20 per cent false negative result for carcinoma of the body of the uterus.[23] There is, however, only a very small percentage of error in the case of positive smears, e.g., 0.04 per cent. In other words, a positive smear means that a cancer is probably present, but a negative smear does not give complete assurance that no cancer is present.

Summary

Prevention rather than early diagnosis should be the primary goal of the general practitioner in any program of cancer control. Office electrocauterization of all chronically infected cervices is an excellent prophylaxis against carcinoma of the cervix. All cases of cauterized cervical erosions which do not heal properly should be considered carcinomatous until proved otherwise. Patients with these unhealed cervical erosions should then be referred to a Diagnostic Cancer Clinic or gynecologist for further tests and study. At that time, a cervical biopsy should be done with the Schiller test to point out areas most suitable for biopsy. The Papanicolaou vaginal smear should be used to complement the cervical biopsy but never to replace it since the expected 10 per cent false negative vaginal smear does not reliably indicate that no cancer is present. Although a positive Papanicolaou vaginal smear suggests that cancer is present, the final diagnosis is dependent on the microscopic examination of the cervical biopsy.

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350 EAST BROAD STREET.

HYPERESTROGENISM AND ITS THERAPY*

Preliminary Report

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IN THE past two decades the results of low estrogen levels in the body have been well recognized and replacement therapy with estrogens used extensively; in fact, more often than not, these patients have been overtreated. The use of this hormone in the menopause and other allied conditions is by this time commonplace therapy.

However, there are many instances in which the level of estrogen in the body is high. This may occur even at the time of the menopause and the use of estrogens is certainly definitely contraindicated and at times quite harmful. We are all familiar with the situation in which the patient has been given estrogen either to be giving something or, more often than not, just because of her age.

The syndrome of hyperestrogenism is one in which the level of estrogen in the body is high and may strangely enough occur at any age period of the patient. A description of a few of the physiological activities of the estrogenic hormone as we know it today follows:

1. Estrogen is a growth hormone. It maintains growth of various parts of the body, especially the genital tract and the secondary sex characteristics.

2. It causes swelling and congestion of the skin of the vulva due to an increase in circulation of this area and the growth of the tissues in general in this region. Pubic hair is usually well developed where the hormone is present in excess.

3. The vaginal mucosa is characterized by excessive growth. The mucosa is thick; it is thrown up into folds as a result of the proliferation of the various layers. Furthermore, as a result of the excessive proliferation, there is extensive shedding of the surface layer of cells so that on examination of the vaginal secretion it has very definite characteristics. The secretion is white, smooth, of even consistency, contains a thin clear mucus and has a pH of around 4 to 4.5 On microscopic examination the secretion shows numerous cornified scale cells (the cells of the superficial layers), very few white blood cells, few bacteria, and usually a thin clear mucus. At times it may be quite excessive and the patient may complain of it, but, in spite of this, she very seldom, if ever, complains of itching or irritation of any type from this particular secretion; in contradistinction to that type of secretion present in infection where the discharge may be very irritating.

4. The effects on the uterus are well observed. The muscle is firm and yet not hard. The uterus is of normal size and may occasionally be slightly

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smaller than normal. The organ may be extremely vascular, the glands increase in size, become hyperemic and frequently show a tendency to slough very readily, giving rise to abnormal uterine bleeding. This occurs especially when the level of estrogen is continuously high in which case there is hyperplasia of the endometrium with vacuolization and subsequently sloughing of the endometrial lining of the uterus. Thus the regularity of the menstrual cycle is frequently interfered with.

5. Estrogen affects the tonicity of the muscles; consequently, the uterine motility is affected. Contractions are increased in frequency and duration, resulting in a tender uterus. These reach a peak just before the onset of the menses. In more severe cases they may be present through the entire menstrual cycle and interval.

6. Estrogen affects the growth and peristalsis of the Fallopian tubes.

7. Estrogen by stimulating muscle also affects the urinary vesicle sphincter, often giving rise to irritation, dysuria, urgency, and the like.

8. Estrogen does not affect the ovary directly but indirectly by acting on the pituitary, in which case the ovary is secondarily involved.

9. Estrogen affects the breast by causing an increase in the growth of the duct system so that the breast becomes large. Circulation is increased and the veins become dilated.

10. The effect on libido is apparently a variable factor.

11. Constitutional effects are well noted with the estrogens. There is an increase in extracellular fluids throughout the entire body.

Noting these few facts concerning the physiology of estrogen the average physician, who is unable to use extensive laboratory procedures, can, by carefully noting the history and observing the various physical findings associated, usually make a diagnosis of hyperestrogenism. It is seldom that all the physical findings and symptoms are present but usually there are a sufficient number so that a diagnosis may be made:

1. One of the most common complaints is premenstrual tension. The patient complains of headache, irritability, she cries easily, she is argumentative, she says she has no patience, she is on edge, and at times may be depressed. This condition usually comes on anywhere from 2 to 10 days before the onset of the menses and eases up with the onset of the flow in most instances. Patients having headaches at other times may state that they are markedly aggravated at this period. They are usually in the frontal and suboccipital regions. When the condition becomes worse this tension instead of coming on from 2 to 10 days before the menstrual period may be present all the time.

2. The patient complains frequently of tender and enlarging breasts. She states that the brassiere causes pain, that the breasts are getting larger. She may notice that the veins are dilated, the nipples larger, and frequently that the Montgomery glands have become enlarged. At times she notices that the breast may become lumpy and it worries her that she may have a tumor mass. This condition, too, usually subsides following the onset of the flow. In the past in many instances a diagnosis of chronic cystic mastitis has been made.

3. The patient may notice that her abdomen is bloated and she will tell you that just before her period her clothes become tighter than usual. Occasionally she comes in for examination thinking she has a bowel upset.

4. At times the patient may complain of variations in the menstrual cycle. The flow may be heavy, it may be scant, the intervals may be close together or may be extended. There seems to be no regularity. The variations probably are due to the manner in which estrogen is secreted. The patient may

be secreting estrogen constantly at a low level which eventually builds up or she may be secreting at a high level which is variable at times giving her variations in the type of menstrual cycle. At times she may have severe cramps (mentioned before) and at other times she may have completely painless menses. In fact this dysmenorrhea is one of the things that commonly brings a patient to the physician.

5. Since high estrogen levels will frequently result in anovulation the patient may come in complaining primarily of sterility.

On physical examination we find the following:

1. The patient may appear tense; she may have a nervous, tense look in her eyes even to the extent of suggesting a hyperthyroid state, and yet when the basal metabolism rate is checked it may be normal or, as it usually is, low. The pain threshold in this patient may be such that a pelvic examination is difficult to perform. Reflexes, when checked may be found to be very active.

2. The breasts are found to be tense, the veins dilated, the breast tissue full, feeling lumpy at times, and as if there are cords present, and extremely tender. At times the breasts have a feeling of warmth, and the nipples are usually enlarged, erect, and tender.

3. The patient may have a suggestion of a subclinical hypothyroid state; by that I mean she may be normal in weight or she may be thin, yet on examination the hair is found to be somewhat dry, the eyebrows a little scanty, the skin dry; all suggesting that she may have a tendency to low thyroid activity.

4. On pelvic examination the pubic hair is usually found to be somewhat heavy. The external genitals are well developed and full due to the edema of the tissue. The clitoris may be normal and sometimes even small in size. The perineal musculature is in good tone and may even be tense. In the vagina the upper third is usually found to be spastic. The rugae of the vaginal wall are high and thrown up into folds, the walls have a feeling of tenseness and tonicity.

The pH of the vaginal secretion is found to be low, around 4 to 4.5, and the secretion may be excessive, and have a smooth consistent feel. There is no irritation of the external skin, no itching of any type. The mucus is found to be usually clear and thin. On microscopic examination the pus cells are usually few, the bacteria are few, and there are many epithelial cells present of the scale or cornified type with few deep cells present. Here again the mucus is found to be thin.

The cervix is frequently normal; erosions, ulcerations, and infections are uncommon, due in part to the fact that the acidity of the vagina is so high, in short, nature is doing for that patient what we attempt to do in treating vaginal infections, that is, giving her a secretion of high acidity. The uterus is usually of normal size, shape, and position. Retroversions are uncommon unless there has been a previous infection since the uterine supporting ligaments are in good tone at all times. Movement of the uterus causes tenderness out of proportion to the efforts required. The ovaries usually are tense, slightly enlarged, and tender. There is frequently a prolapse to some degree of the right ovary. In instances in which retrodisplacements are present, due to previous disease, the ovaries may be quite large because of the

congestion and all symptoms are appreciably aggravated. The bladder trigone is frequently tender due to the excessive congestion present. Basal temperature charts will often show cycles of anovulation.

On the basis of these symptoms and findings a working diagnosis of hyperestrogenism can be made in many instances.

Treatment revolves itself about the depression of the estrogenic activity of the ovaries; in other words, the administration of preparations referred to as "anti-estrogens."

One of the most common and efficient preparations is thyroid. The dose in this case need not be large and should be given over a period of at least two months or more before its effect can be evaluated, since the effect on the ovary is slow. The first month the patient may notice no change; the second month she may notice some change, and then improve gradually. This drug of course is of special help in those conditions in which we suspect hypothyroid states.

The drug, however, I find to be of best use is the male hormone, testosterone. I have found this to be consistently good, although I use other preparations in conjunction with it. I find that it works best in the oral form, methyl testosterone, in doses of 10 mg. daily, given usually at bedtime. I am careful to remind my patients that for at least two months they will notice little change; in short, the first menstrual period may be just as severe as the previous one. At the end of two months, if the drug is going to work, we shall expect improvement. I have not seen any appreciable ill effects at this dosage level if the patient is watched carefully. I am very careful to remind patients that as long as they are taking the drug they should be under constant observation. Only occasionally at this dosage level do I find any acne, excessive hair growth, or deepening of the voice. If the patient is seen at frequent intervals the drug may be stopped at once and no harm done. The work of Hellbaum indicates that this hormone apparently acts by effecting the release of the pituitary luteinizing factor.

In those few instances in which the male hormone is not tolerated progesterone may be substituted either hypodermically or in the oral form. I find this to be effective but not nearly so much so as the male hormone. Then, too, the effect is purely replacement since, when the drug is stopped, the symptoms recur, whereas, with the male hormone, the patient, after taking the male hormone from two to three months, may go for a period of six to eight months without recurrence. Only occasionally do we have to keep the latter drug continued at a smaller dose level. The doses of progesterone hypodermically vary from 10 to 20 mg. intramuscularly several times a week. If results are obtained this is followed with the oral form in doses of 25 to 50 mg. daily. In both instances (with testosterone and progesterone) I find that I get the best results by giving the drug continuously, that is, throughout the entire cycle. At one time I gave larger doses beginning 10 days before the menstrual period but the patient did not have the sense of well-being at other times of the cycle that is obtained by this method.

Chorionic gonadotrophin is of help at times since it causes regression of the ovary but should be used with caution.

In those instances in which retrodisplacement of the uterus is present the knee-chest position by improving circulation in the uterus and ovaries may help in addition to the previously described medication.

In short, I believe the treatment, when it is once begun, should be continued steadily without interruption for at least two months before the results are evaluated. In many instances the results are dramatic and may last, as mentioned above, from six to eight months or longer before signs of recurrence appear. In those cases the routine may be repeated without difficulty. There are of course instances in which there is no improvement. In many cases I find the diagnosis to be probably wrong; that what I thought was hyperestrogenism was a disturbance from some other source, as for example, some previous infection. Patients should be warned not to repeat medication of their own accord. In many instances because of the excellent relief of pain, patients will have their prescriptions refilled and keep taking the drug indefinitely. I constantly remind these patients that as long as they are taking this treatment they should be under the constant care of a physician.

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METHERGINE: A STUDY OF ITS VASOMOTOR PROPERTIES

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IN A previous clinical study[1] Methergine, a partially synthetic ergot alkaloid, prepared by Stoll and Hofmann[2] from lysergic acid to form d-lysergic acid-dl-hydroxybutylamide-2, was found to be an effective oxytocic, as judged by prompt uterine contraction, short third stage of labor, and satisfactory postpartum blood loss. The pharmacology of Methergine was studied by Rothlin[3] and Kirchhof and associates.[4, 5] Numerous papers have appeared dealing with the favorable oxytocic properties of Methergine and this report concerns itself mainly with the clinical vasomotor properties of the drug. The earlier publication[1] did not include an evaluation of the blood pressure response but the impression was that the vasopressor phenomena were infrequent when Methergine was employed.

Material

The present study was undertaken to determine what, if any, vasomotor reactions were to be expected following the intravenous use of Methergine. Particular attention was paid to those patients with a clinical history of hypertension during the current pregnancy, and to those patients admitted with blood pressure above 140 mm. hg systolic and/or 80 mm. diastolic.* The series consisted of two groups of 200 patients each, one group receiving 0.2 mg. of Methergine† intravenously and the other group 0.2 mg. ergonovine intravenously. Although neither group is large, it was felt that a sufficient number of patients was studied to reach valid conclusions. In both series, consecutive cases were used, with the only selectivity being that vaginal deliveries were considered. Both private and clinic patients were evaluated in this study.

Age distribution was almost identical in both groups. In the Methergine series the spread was from 16 to 41 years, the average 28.5 and the mean 27, while the ergonovine group ranged from 15 to 43 years, the average 29 and the mean 26 years.

A close parallelism is shown in Table I between the two groups in relation to the number of pregnancies.

The similarity between the two groups is further emphasized by a comparison of the methods of delivery, as shown in Table II.

Spinal anesthesia was used in 133, or 66.5 per cent, of the Methergine group and in 148, or 74.0 per cent, of the ergonovine patients. Gas-oxygen-ether was the anesthetic for 63, or 31.5 per cent, of the Methergine group and for 51, or 25.5 per cent, of the ergonovine group.

Hemorrhage (loss of more than 500 c.c. of blood) occurred in 3 of the Methergine patients and in 4 of the ergonovine patients.

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*Throughout the study, an increase of 20 mm. Hg in either the systolic or diastolic pressure was considered to be significant.

†The Methergine was supplied by Sandoz Pharmaceuticals, San Francisco, Calif.

Management of the third stage was by manual removal of the placenta in 4 of the Methergine and in 7 of the ergonovine patients.

During this study, the admission blood pressure was used as the base line. For purposes of checking the blood pressure reaction to the drugs used, the pressure was taken at intervals of one, five, fifteen, thirty, and sixty minutes after the drugs were given intravenously.

TABLE I

GRAVIDA	METHERGINE		ERGONOVINE	
1	83	41.5%	87	43.5%
2	69	34.5%	63	31.5%
3	35	17.5%	30	15.0%
4	8	4.0%	11	5.5%
5	1		5	
6	2		3	
7	1		0	
8	1		0	
9	0		1	
Total	200		200	

TABLE II

METHOD OF DELIVERY	METHERGINE		ERGONOVINE	
	NUMBER	PER CENT	NUMBER	PER CENT
Spontaneous	61	30.5	59	29.5
Forceps	124	62.0	128	64.0
Breech	8	4.0	4	2.0
Forceps rotation	7	3.5	8	4.0

History of Hypertension

In this study, the upper limits of normal blood pressure were considered as 140/80. Nine of the Methergine group gave a history of hypertension at some time during the pregnancy, and 10 of the ergonovine group gave such a history.

Of the 9 patients with such history who received Methergine, 6 patients had an admission blood pressure above 140 systolic, and 4 had a diastolic pressure above 80. Six (66.6 per cent) of the 9 patients had no significant increase of blood pressure after administration of the drug. Included in this group were 4 of the 6 whose admission systolic rate was over 140 and all of the 4 whose diastolic pressure was above 80. Two patients (22.2 per cent) had a significant rise of the pressure after Methergine was given, both of whom had admission systolic pressures over 140. In both of these cases, the increase was in the diastolic pressure and occurred within one minute of administration of the drug. The maximum rises were 25 and 30 mm. hg, respectively. One patient was admitted with a pressure of 130/78. Prior to her spinal anesthetic, the pressure rose to 168/68, and then progressively dropped to the admission level.

Of the 10 patients with history of hypertension who received ergonovine only, 3 on admission had systolic pressures above 140, and 6 had diastolic pressures over 80. Four (40 per cent) of the 10 patients had no significant increase of blood pressure after the drug was given, whereas 6 (60 per cent) had a significant rise. In 4 of these 6 cases, the pressure had increased significantly within one minute; in 3 the increases were systolic and in one diastolic. In the other 2 patients who had increased blood pressure levels, the increase occurred at fifteen minutes, and was represented by systolic increase in one case and

diastolic in the other. The maximum systolic rise was 42 mm. and the greatest diastolic rise was 38 mm. Of the 6 patients who had significant increases of blood pressure, only one had an admission pressure of over 140 systolic. Two patients had elevation of diastolic pressure only on admission.

Table III summarizes the findings in the group with a history of hypertension during the pregnancy.

TABLE III. PATIENTS WITH HISTORY OF HYPERTENSION

	METHERGINE		ERGONOVINE	
Admission systolic over 140	6		3	
Increased after drug		0		1
No increase after drug		6		2
Admission diastolic over 80	4		6	
Increased after drug		2		2
No increase after drug		2		4
Admission systolic under 140	3		7	
Increased after drug		0		5
No increase after drug		3		2
Admission diastolic under 80	5		4	
Increased after drug		2		2
No increase after drug		3		2

No History of Hypertension

Of the Methergine group, there were 32 patients who gave no history of hypertension, but who had blood pressure of 140 systolic and/or 80 diastolic, or above, on admission. Of these, 2 (6.25 per cent) had an increase of the pressure after the drug was given, and 30 (93.75 per cent) had no increase. There remained 159 patients without history of hypertension and with normal blood pressure on admission, of whom 18 (11.3 per cent) had a significant increase of pressure after the drug was given. Twenty patients with no history of hypertension had significant increases of the blood pressure, a percentage of 10.4. The greatest number, 8, occurred at one minute, with 6 at five minutes, 4 at fifteen minutes, and 2 after thirty minutes. The systolic pressure alone was increased in by far the greatest number, 16. Diastolic only was increased in 3 patients, while 2 patients had both systolic and diastolic pressures increased.

In the ergonovine group, there were 38 patients without hypertension history, but with elevated blood pressure on admission. Five of these patients (13.1 per cent had increases of pressure after administration of the drug. There were 152 patients without history of hypertension and with normal blood pressure on admission, and of this group, 48 (31.6 per cent) had significant increases of blood pressure after the drug. Of the patients with no history of hypertension, 53 (27.9 per cent) had increased blood pressure after being given ergonovine. The greatest number of increases, 26, occurred at one minute, closely followed by 21 at five minutes, with 5 at fifteen minutes, 3 at thirty minutes, and 4 at one hour. These figures are for the total number of ergonovine-treated patients who had increased blood pressure after the drug was given. The systolic pressure alone was increased in 35 cases, the diastolic only in 4 cases, and both systolic and diastolic in 20 cases. Table IV summarizes the groups which had no history of hypertension.

In the Methergine group, there was a total of 22 patients (11 per cent) who had increased blood pressure after the drug was given. For ergonovine patients, the total was 59, or 29.5 per cent.

None of the Methergine-treated patients developed convulsions, although in one case the pressure rose to 200/110 one hour after the drug was given.

There was no history of hypertension and the admission pressure was 130/80. The patient was 30 years of age, gravida vi.

One patient in the ergonovine series developed convulsions on the first postpartum day. There was no history of hypertension and the admission pressure was 130/90. She was 34 years of age, and was delivered of twins.

TABLE IV. PATIENTS WITH NO HISTORY OF HYPERTENSION

	METHERGINE		ERGONOVINE	
Admission pressure above 140 and/or 80	32		38	
Increased after drug		2 (6.25%)		5 (13.1%)
No increase after drug	30		33	
Admission pressure below 140 and/or 80	159		152	
Increased after drug		18 (11.3%)		48 (31.6%)
No increase after drug	141		104	

Summary

To determine what effect Methergine has on the blood pressure of the immediately postpartum patient, a series of 200 consecutive patients was studied. A group of 200 patients who received the usual ergonovine was used as controls. All patients were delivered vaginally and all received the drug intravenously. A striking similarity between the two groups is shown by a comparison of age distribution, parity, method of delivery, and anesthetic used. The average age of the Methergine patients was 28.5 years and that of the ergonovine patients was 29 years. In the Methergine group, 41.5 per cent were gravida i and 34.5 per cent were gravida ii; in the ergonovine series, the figures were 43.5 per cent and 31.5 per cent, respectively. Delivery was spontaneous in 30.5 per cent of the Methergine patients and 29.5 per cent of the ergonovine patients; by forceps for 62 per cent of the Methergine group and 64 per cent of the ergonovine group.

A history of hypertension during the pregnancy was found in 4.5 per cent of the Methergine patients and in 5.0 per cent of the ergonovine patients. In the Methergine group, 22.2 per cent had significant rise in blood pressure after the drug was given and in the ergonovine group 60 per cent had increases. Methergine apparently is more likely to cause the diastolic pressure to rise, while ergonovine seems to affect the systolic pressure more frequently. With both drugs, the blood pressure effect is very rapid, occurring within one minute of administration in most cases. Excluding those cases in which large amounts of blood were lost, in neither of the two groups did the drug cause a drop in blood pressure.

In the Methergine group, of the patients without history of hypertension, 32 had abnormally high blood pressure on admission, and in the ergonovine group, 38 patients had elevated blood pressure on admission. After Methergine was given, 6.25 per cent had increased blood pressure and after ergonovine 13.1 per cent had elevated blood pressure.

Of the patients with no history of hypertension and normal blood pressure on admission, the blood pressure was increased in 11.3 per cent of those who received Methergine and in 31.6 per cent of those who were given ergonovine.

With both drugs, blood pressure elevations usually occurred within five minutes of the administration of the drug. The systolic pressure was increased much more frequently than the diastolic.

For the entire group of patients who received Methergine, 11 per cent had significant blood pressure elevations following administration of the drug, whereas 29.5 per cent of those who received ergonovine had a significant rise.

Conclusions

Methergine seems to be much less prone to have a vasopressor action as one of its side effects than some other oxytocics.

For the entire series, a significant blood pressure increase was found in 11 per cent of the Methergine patients as compared to 29.5 per cent of the controls.

In those patients with no history of hypertension during the pregnancy and with normal blood pressure on admission, 11.3 per cent of the Methergine group developed increased blood pressure and 31.6 per cent of the control group.

Oxytocics can be given with comparative safety to patients with abnormally increased blood pressure. Six and twenty-five hundredths per cent of the patients with no history of hypertension but with blood pressure over 140/80 on admission had a significant rise of the pressure as compared to a rise in 11 per cent of those with normal pressure, when Methergine was used. When ergonovine was used, the figures were 13.1 per cent and 29.5 per cent for the two categories. For both drugs, the rate was lower in the hypertension group than in the "normal" group, and with Methergine there was a much lower rate in both categories.

Patients with histories of hypertension during the pregnancy develop increased blood pressure about twice as often as those with no such history, 22.2 per cent against 11.3 per cent in the Methergine series and 60 per cent against 31.6 per cent in the ergonovine series. Methergine is much safer in these patients, almost three to one, 22.2 per cent as compared to 60 per cent.

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CORRELATION OF WEIGHT, LENGTH, AND TIME FACTORS IN FETAL AGE

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IN READING the pediatric and obstetric literature relative to abortions and premature births, we have observed that there is considerable lack of uniformity in the classification of cases. Various writers use quite different standards for determining fetal age at the time of birth. It is obviously impossible to make any true comparison between results reported by different clinics or even results from the same clinic at different times unless the same standard of classification is used throughout. It would appear that a uniform standard for classifying cases would allow direct comparison of results. This in turn would give a true evaluation of the methods employed. Wider application of the most successful methods would in turn contribute directly to a greater salvage of premature babies, a category where there is room for considerable improvement.

The authors do not presume to offer an arbitrary new standard, but will try to correlate data which has long been accepted as reliable. An attempt will be made to present this in a practical workable arrangement which can be used to determine the stage of gestation at which pregnancy was terminated. When employed, this standard will group together babies of similar development. Significant variations in clinical results will then more truly reflect the quality of neonatal care given.

Such classification would in borderline cases give a more specific basis for compliance with the legal requirements of birth and stillbirth registration. It would also be of value in the classification and analysis of obstetrical statistics relative to maternal morbidity and mortality.

The existing standards for weight and length of the fetus at various months of gestation are based on averages from large series of cases. They are generally accepted and are a logical basis from which to develop a more detailed and workable standard.

Weight

Weight is the factor most frequently considered in discussing development of the fetus. Table I gives the average weight by lunar months as reported by two different investigators and quoted by standard textbooks as acceptable.

TABLE I. WEIGHT OF THE FETUS IN RELATION TO AGE

LUNAR MONTH	STREETER[1] (GRAMS)	SCAMMON AND CALKINS[2] (GRAMS)
2	1.0	3.5
3	14.2	14.3
4	108.0	86.8
5	316.0	260.9
6	630.0	551.6
7	1,045.0	971.4
8	1,680.0	1,519.0
9	2,478.0	2,196.1
10	3,405.0	2,998.8
Postmature		4,500.0[5]

Length

Length is the next most important factor for consideration. The over-all (crown-heel) length is most commonly used. Table II gives the crown-heel length by lunar months as reported in the literature.

TABLE II. LENGTH OF THE FETUS IN RELATION TO AGE

LUNAR MONTH	DIETRICH[3] (CM.)	SCAMMON AND CALKINS[2] (CM.)	HAASE'S RULE[4] (CM.)
2	3.0		4
3	9.8	7.0	9
4	18.0	15.5	16
5	25.0	22.7	25
6	31.5	29.2	30
7	37.1	35.0	35
8	42.5	40.4	40
9	47.0	45.4	45
10	50.0	50.2	50
Postmature			54[5]

Time

Time from the last menstrual period is the third factor and the one most frequently used. However, it is probably the least reliable of all in the accurate determination of fetal age.

A more accurate appraisal of fetal development would seem to be obtainable by the use of a classification rule which gives consideration to all three factors. This is what we propose.

In developing a practical standard for clinical use the figures shown in Tables I and II were plotted graphically against time. From these graphs, values for weight and length were determined by weekly intervals.

The dividing line between "immaturity" (prematurity) and "maturity" has been established by the *International Statistical Classification of Diseases, Injuries and Causes of Death* (6th Revision, 1948) as 5½ pounds (2,500 grams) or 37 weeks of gestation. This fixed point must, of course, be observed. It fits in nicely with the data obtained as described above.

Working then on the basis of weeks from the last menstrual period, it is possible to arrange a table of values showing the correlation between weeks, calendar months, lunar months, weight, and length. In addition, landmarks in the progress of pregnancy such as quickening, viability, and maturity can be indicated. These in turn mark the separation in to the clinical classifications of early abortions, late abortions, and births. The births are further divided into 7 month premature, 8 month premature, term, and postmature.

TABLE III. FETAL AGE TABLE

| WEEKS | WEIGHT | | MONTHS | | LENGTH | | WEEKS | LAST MENSTRUAL PERIOD |
	GRAMS	LB., OZ.	CALENDAR	LUNAR	CM.	INCHES		
1							1	
2							2	CONCEPTION
3							3	
4			1	1	1		4	
5							5	
6							6	
7							7	
8	1			2	4	1½	8	Early abortions
9	2		2		5.2	2	9	
10	4				6.5	2½	10	
11	7				7.7	3	11	
12	14	½		3	9	3½	12	
13	25		3		10.7	4¼	13	
14	45				12.5	5	14	
15	70				14.2	5½	15	Abortions
16	100	3		4	16	6¼	16	
17	140				18	7¼	17	
18	190		4		20.5	8	18	
19	240				22.8	9	19	
20	300	10	4½	5	25	10	20	Quickening
21	375	13				10½	21	
22	450	1	5		27.5	11	22	Late abortions
23	525	1 3				11½	23	
24	600	1 5	5½	6	30	12	24	
25	700	1 9				12½	25	(Previable prema-
26	800	1 12	6		32.5	13	26	ture)
27	900	2				13½	27	
28	1,000	2 3	6½	7	35	14	28	Viability
29	1,150	2 9				14½	29	
30	1,300	2 14	7		37.5	15	30	7 month premature
31	1,450	3 3				15½	31	
32	1,600	3 8		8	40	16	32	
33	1,775	3 15	7½			16½	33	
34	1,950	4 5			42.5	17	34	8 month premature Births
35	2,125	4 11	8			17½	35	
36	2,300	5 1		9	45	18	36	
37	2,500	5 8	8½			18½	37	Maturity
38	2,800	6 3			47.5	19	38	
39	3,100	6 13	9	10	50	19½	39	Term births
40	3,400	7 8				20	40	
41	3,750	8 4	9½			20½	41	
42	4,100	9 1			52.5	21	42	
43	4,500	9 15	10		54	21½	43	Post mature

These various factors are brought together in the Fetal Age Table (Table III). This table is proposed as a standard to be used in the classification of cases. From the pediatric viewpoint it will group cases on the basis of relative maturity, and obstetrically it will give a clinical grouping of cases that will facilitate study and analysis.

Age in weeks can be read directly from the fetal age table for both weight and length of the infant. These two figures along with the actual weeks since the last menstrual period are used to determine fetal age.

The fetal age in any given case will be determined by two of the three factors just listed. If all three are different they should be averaged and fetal age designated as that week closest to the average.

If the last menstrual period is unknown or appears to be grossly out of line it should be disregarded and fetal age determined by weight and length alone.

These figures refer primarily to single births. Babies from multiple births are probably more mature than their size would indicate. Even so, it would seem wise to classify and treat them on the basis of size until their maturity and ability to survive are definitely established.

In addition to the more accurate determination of fetal age from an academic and statistical point of view, the table would be of value in determining the reportibility of the case. The *Physician's Handbook on Death and Birth Registration* (1949) published by the National Office of Vital Statistics, United States Public Health Service, gives the following definitions pertaining to the reporting of births:

Live births: A child showing any evidence of life (action of heart, breathing or movement of voluntary muscles) after complete birth should be registered as a live birth.

Stillbirth: A fetus showing no evidence of life after complete birth, if the twentieth week of gestation has been reached, should be registered as a stillbirth.

However, reportability varies according to the laws in the individual states. It is the physician's responsibility to familiarize himself with the law on vital statistics of the state in which he practices. He should report his cases accordingly.

Summary

Attention is called to the need for greater uniformity in classification of births according to fetal development.

A table is presented which correlates the various factors of weight, length, and time with accepted clinical groupings of fetal development.

Procedure is suggested for the use of this fetal age table in properly classifying the individual infant according to his development.

It is suggested that this fetal age table be used as a standard by those analyzing results in obstetrics, and the closely related subject of pediatric care of the premature infant.

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14805 DETROIT AVENUE

CHANGING TRENDS IN CESAREAN SECTION

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THIS survey of cesarean section operations from the public and private patient obstetrical records of the Toronto General Hospital was undertaken for two reasons: first, to record and compare the incidence and maternal mortality of cesarean section in public and private ward practice over a fifteen-year period, 1935 to 1949, and second, to make a more detailed analysis of public ward cesarean sections over a twenty-five-year period, 1925 to 1949, as to changing trends in incidence, indications, type of operation, and maternal and fetal mortality.

TABLE I

	DELIVERIES	SECTIONS	INCIDENCE	MORTALITY
Public.—				
1935-1949	13,728	294	2.14	1.02%
1925-1934	7,423	250	3.36	4.40%
Private.—				
1935-1949	18.005	1,166	6.4	0.8%
Totals	39,156	1,710	4.37	1.28%

While the public ward survey covered a twenty-five-year period, 1925 to 1949, the private ward survey covers only the last fifteen years of that period. It will be noted that the incidence of cesarean section in the public ward series dropped from 3.36 per cent during the first ten years to 2.14 per cent the last fifteen years. This 2.14 per cent incidence for the public ward series is in marked contrast to the 6.4 per cent incidence in the private ward series for the same fifteen year period, 1935 to 1949. There are many factors which tend to produce this higher incidence in the private wards as compared to that in the public wards. It is easier for group or staff consultation to carry the patient through a difficult labor than it is for the individual obstetrician. The latter is more subject to pressure from patient and family in the early stage of difficult labor because of the direct responsibility which he has to assume. Among private patients, there is also, because of social and economic conditions, a tendency to limitation of the number of pregnancies. Most private patients are well aware that with the increasing safety of the operation of cesarean section they can usually look forward to at least three children by this method. The individual obstetrician is also very anxious to avoid the possibility of stillbirth from a long and difficult labor which in all probability will also entail considerable maternal soft-tissue trauma.

The maternal mortality in the latter fifteen-year (1935 to 1949) period of the public ward series showed a sharp reduction to 1.02 per cent as compared to 4.4 per cent in the first ten-year (1925 to 1934) period. Eleven of the total of fourteen deaths occurred in the first ten-year period. However, in the same fifteen-year period, 1935 to 1949, the private ward series showed a still lower maternal mortality rate of 0.8 per cent in spite of a markedly increased incidence rate as compared to the public ward series. This is striking evidence of the steadily lessening risk attending the present-day operative delivery by cesarean section.

One may also survey the twenty-five year period of public ward patients and discover some changing trends as to type of operation employed as well as some marked changes in the indications accepted for operation.

It is apparent that the low segment operation has almost entirely replaced the classical section. The incidence of Porro section is somewhat reduced and

the extraperitoneal type of section has to some extent been used where Porro section was formerly employed.

If one takes the last five years of the series, 1945 to 1949, it is observed that the trend way from classical section to almost routine employement of low section is very evident. Out of 114 sections done during this period there were only 2 classical sections (1.7 per cent) whereas there were 100 low sections (88.5 per cent). The extraperitoneal type of operation appears occasionally and Porro section remains about 8 per cent of the total incidence.

TABLE II

	CLASSICAL	LOW	PORRO	EXTRAPERITONEAL
10 years.—				
1925-1934	44.7	44.3	11.0	0.4
15 years.—				
1935-1949	25.5	66.6	7.1	0.8
5 years.—				
1945-1949	1.7	88.5	8.8	1.0

Our views as to proper employment for each type of cesarean section might be stated as follows:

1. The low segment operation will be employed almost routinely for all elective sections and for patients who have had a test of labor within reasonable limits.

2. Porro section will be employed in cases of ruptured uterus, neoplasms, and fulminating types of accidental hemorrhage.

3. Classical section will be used only in certain cases of election where speed of delivery is considered necessary in the interests of mother and child, or where local conditions found on opening the abdomen, such as adhesions from previous operations, make employment of the low segment incision inadvisable. The high incision will, of course, often be used prior to hysterectomy.

4. Extraperitoneal section will be the operation of choice in neglected cases in labor over 48 hours. Following an unduly prolonged test of labor it will, on infrequent occasion, from lack of further progress, be found necessary to reverse the decision for vaginal delivery in favor of extraperitoneal section. It may be suspected that, in an area where frequent employment of extraperitoneal section is found necessary, the obstetrical supervision of such patients is not efficient. The safety from sepsis of extraperitoneal operations must not be allowed to condone poor supervision of labor in its early stages.

In a survey of the changing trends in indications for cesarean section in this twenty-five years period one may note that, in the last fifteen-year period as compared to the first ten-year period, the indications of disproportion and ruptured uterus remain about the same. The indications of previous section, placenta previa and diabetes show an increase, whereas the indications of accidental hemorrhage, pre-eclamptic toxemia, and tumor have decreased slightly. Rheumatic heart disease, which appeared as an indication in 14.8 per cent of the series 1925 to 1934, has, since then, entirely disappeared as an indication per se. This, in brief, has been the changing trend as regards indications for cesarean section in our series.

It will be noted that eleven of the total fourteen maternal deaths occurred in the first ten-year period. There has been a marked reduction in mortality during the latter fifteen-year period to 1.02 per cent. In fact the three maternal deaths, 1935 to 1949, all followed Porro sections and there have been 276 consecutive classical and low segment sections performed in this period without maternal mortality.

TABLE III. INDICATIONS, PUBLIC WARDS

	1925-1934 250 SECTIONS %	1935-1949 294 SECTIONS %
Disproportion	34.4	30.3
Previous section	20.4	41.0
Placenta previa	10.8	13.2
Accidental hemorrhage	3.2	2.0
Pre-eclampsia	8.4	2.0
Tumor	2.0	1.0
Ruptured uterus	1.2	1.0
Diabetes	0.0	1.7
Heart disease	14.8	0.0
Miscellaneous	4.8	5.8

TABLE IV. MATERNAL MORTALITY

YEARS	SECTIONS	DEATHS	% MORTALITY
1925-1934	250	11	4.4
1935-1949	294	3	1.02

The fetal stillbirth and neonatal mortality accompanying cesarean section remains high, averaging nearly 15 per cent. Of this over-all fetal mortality, about two-thirds is due to stillbirth and one-third to neonatal deaths. The still-births for the most part were due to prematurity, accidental hemorrhage, ruptured uterus, placenta previa and fetal deformities.

TABLE V. STILLBIRTH AND NEONATAL MORTALITY

	SECTIONS	STILLBIRTH AND NEONATAL MORTALITY	%
10 years 1925-1934	250	41	16.4
15 years 1935-1949	294	39	13.3

Summary

1. A survey is made of 1,710 cesarean sections occurring in 39,156 public and private ward deliveries in the Toronto General Hospital.

2. Public and private incidence and mortality are compared.

3. A more detailed survey is made of 544 sections in 21,151 deliveries in the public ward service over a twenty-five year period as to changing trends in indications, and the type of operation employed.

4. Maternal mortality rate shows marked reduction.

5. The still birth and neonatal mortality during this twenty-five year period is noted and that of the last fifteen-year period compared with that of the first ten-year period.

6. From the almost routine use of the low segment operation without mortality to the exclusion of the classical section, one might infer that with proper conduct of test labors it should not be necessary to employ the extraperitoneal type of operation except in those cases where supervision of labor has been grossly inefficient.

714 MEDICAL ARTS BUILDING

TREATMENT OF THE SURGICAL MENOPAUSE WITH ESTRADIOL PELLETS AT THE TIME OF OPERATION*

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MEDICAL literature contains many papers dealing with the treatment of estrogen deficiency by the subcutaneous implantation of estradiol pellets.[1,2,3] In one of the more recent studies Perloff[3] reported that he was able to achieve complete relief of symptoms in 96 of 100 hypogonadal or menopausal women, with average duration of relief of 7.2 months (one pellet) and 8.4 months (2 pellets). These excellent results suggested the possibility of delaying or eliminating the symptoms of the surgical menopause by the implantation of estradiol pellets at the time of operation.

Material and Results

In this series of patients, either one or two 25 mg. estradiol pellets were implanted subcutaneously, superior and lateral to the upper angle of the abdominal incision in consecutive, unselected women undergoing hysterectomy and bilateral salpingo-oophorectomy. The control group comprised all patients who had ovariectomies at the Philadelphia General Hospital during 1947.

Table I gives the essential data. Of 54 patients in the control group, 37 were available for follow-up. The age range of this group was 20 to 66 years, with an average age of 42.8 years. Menopausal symptoms (vasomotor) appeared for the first time between one and thirty-two weeks following operation with an average of 7.5 weeks. Eight patients had no menopausal complaints postoperatively and of these 5 were postmenopausal at the time of operation. One patient was in the menopause and her symptoms were unchanged postoperatively.

Two estradiol pellets were implanted in 28 consecutive, unselected patients at the time of operation. Follow-up was available in 26. The ages in this group ranged from 23 to 48 years with an average of 38.3 years. The onset of symptoms was appreciably delayed; 8 patients began to have hot flushes between 11 and 17 months postoperatively (average 14.4 months); 18 were still symptom free as long as 10 to 19 months postoperatively (average 14.9 months).

In 17 additional patients one estradiol pellet was implanted at operation. Follow-up was available in 12 of them. The age range in this group was 15 to 48 years (average 40 years). Here again, the onset of symptoms was greatly delayed when compared with the control group, symptoms appearing within 7 to 9 months after operation (average 8 months) in 3 patients. Nine patients were still symptom free from 5 to 12 months postoperatively (average 9.2 months).

There was no wound complication attributable to pellet implantation. Histologic examination of the organs removed surgically revealed no malignancy or endometriosis.

TABLE I. PATIENTS WITH AND WITHOUT ESTRADIOL PELLETS AFTER OVARIECTOMY

	CONTROL	TWO PELLETS	ONE PELLET
No. of Patients	54	28	17
Follow-up	37	26	12
Age range	20 - 66 years.	23 - 48 years.	15 - 48 years.
Average age	42.8 years.	38.3 years.	40.0 years.
Onset of symptoms	29 patients 1-32 (average 7.5) weeks.	8 patients 11-17 (average 14.4) months.	3 patients 7-9 (average 8) months.
Symptom free	8 patients 5 postmenopausal	18 patients 10-19 (average 14.9) months.	9 patients 5-12 (average 9.2) months.

Comment

It appears that the subcutaneous implantation of estradiol pellets at the time of operation is an effective method of delaying and perhaps eliminating symptoms of the surgical menopause. At the last follow-up, as late as 16 to 19 months postoperatively, 9 patients in the treated groups were still asymptomatic. Experience has shown that even when symptoms did appear in the treated patients, the flushes were of milder nature and less frequent occurrence than those experienced by the patients in the control group.

Fortunately, no malignancies were encountered in this series of patients. In the present state of our knowledge concerning the possible carcinogenic effect of estrogens in the human being, it would be unwise to implant estrogen when the suspicion of malignancy exists. All specimens should be carefully examined at the time of operation and, if malignancy cannot be definitely ruled out, the implantation of pellets should be deferred until a histologic report is obtained. Furthermore, since cervical stump carcinoma does occur with tragic frequency, pellet implantation should be reserved for cases in which complete hysterectomy is performed. The presence of endometriosis, chronic mastitoides or suspected breast malignancy is definite contraindication to the use of pellets. Obviously pellet implantation is not necessary or advised in patients who are postmenpausal at the time of operation.

Summary

1. The results of implanting estradiol pellets in the abdominal wound at the time of operation in 38 consecutive, unselected patients undergoing hysterectomy and bilateral salpingo-oophorectomy are described.

2. Comparison with a control group of 37 patients shows that this procedure is an effective method of delaying, ameliorating, and perhaps eliminating the surgical menopause.

3. The major contraindications are discussed.

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THE VOLUMETRIC CAPACITY OF THE HUMAN NULLIPAROUS UTERUS

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THE early anatomists were fully aware of the limited capacity of the human uterus in its virgin state in comparison with the size of the organ itself. They described the uterine cavity as "a mere slit, flattened anteroposteriorly." They noted the triangular shape of the potential space, known as the uterine cavity, the base being formed by the internal surface of the fundus between the openings of the uterine tubes, and the apex by the opening of the internal os. No data have been found in the early writings relative to the actual volumetric capacity of the virgin uterus.

In an effort to record the volumetric capacity of the average nulliparous human uterus, the author has undertaken a study of the uterine cavities of a large number of women. Reynolds[1] has pointed out that, in reality, no two human uteri are exactly alike, but that in general they conform to certain definite patterns. To avoid complications in clinical hysterosalpingography, the following technique was employed, in order to determine, on a scientific basis, the actual capacity of the average nulliparous uteri.

Technique

The genital tracts of 800 previously infertile and nulligravid women were studied in the present series.

By means of a specially devised insufflation instrument,[2] the Gynograph* (which encompasses a calibrated reservoir containing Iodochlorol, a luminescent manometer, and a source of constant pressure), measured amounts of the radiopaque substance were instilled into the uterus, under constant visualization by means of fluoroscopy. Note was taken of the quantity of oil required to fill the individual uterus prior to the flow of the medium into the Fallopian tubes.†

The uterine cavities varied in character from small atrophic spaces holding no more than 0.5 c.c. of oil, to those retaining as much as 3.5 c.c. before tubal visualization. Cases in which bilateral tubal closure was found were not included in the present series since, owing to uterotubal blockage, the uterine cavities necessarily became distended with oil, thus increasing the potential volume capacity of the uterus. Uterine cavities showing evidence of intrauterine fibroids and polyps were also omitted from this study, as well as an occasional uterus didelphys, etc.

During the collating of the data, it became apparent at the outset that the uterine cavities of these women could be classified, according to size and volumetric capacity, into the following three general groups:

Group I	Atrophic (small uterine cavity)	27 cases
Group II	Normal (average uterine cavity)	739 cases
Group III	Hypertrophic (enlarged uterine cavity)	34 cases

*Gynograph manufactured by Goodman-Kleiner Company, New York.

†Allowances were made in each case for the 0.4 c.c. volume of the cannula tube utilized in these studies.

Since these patients were seen primarily as sterility cases, it should be pointed out that the uterine cavities in Groups I and III might necessarily be larger than would be found in a group of fertile nulliparous women. The atrophic and hypertrophic groups can be readily dismissed here by stating that the average ranges were 0.2 to 1.0 c.c. for the atrophic, and 2.4 to 3.0 c.c. for the hypertrophic group. In order to record normal averages, only 739 women who showed so-called "normal" uterine cavities are included in detail in this study.

TABLE I

CLASSIFICATION	VOLUME REQUIRED TO FILL UTERUS (C.C.)	NO. OF CASES STUDIED
Atrophic	0.2	27
	0.4	
	0.6	
	0.8	
	1.0	
Normal	1.2	50
	1.4	136
	1.6	183
	1.8	211 739
	2.0	98
	2.2	61
Hypertrophic	2.4	34
	2.6	
	2.8	
	3.0 and upward	

As will be seen from Table I, the mean average volume required to fill a nulliparous uterine cavity in these 739 cases was 1.7 c.c. Observation of the opaque substance from its entrance into the Fallopian tubes until the evidence of intraperitoneal spillage revealed that an additional 1.0 to 1.5 c.c. was required in the majority of cases. Proportionately smaller quantities were required to fill a single tube in instances of unilateral tubal patency.

Comment

It is apparent that the uterine cavity and the Fallopian tube tracts are but potential spaces requiring an average of 3 to 4 c.c. of iodized oil for outlining. Routine hysterosalpingography in clinical practice should provide for the instillation of these small quantities and thus eliminate the injection of excessive amounts of foreign material.

With the use of hysterosalpingography and the instillation of viscous radiopaque substances into the uterotubal tract, many physicians have apparently lost sight of the fact that the cavity of the nulligravid woman is actually not a true cavity, but merely a potential slitlike space. Brown, Jennings, and Bradbury[3] instill from 8 to 12 c.c. of opaque material into the uterus for uterotubal x-rays. Unnecessary retention of excessive amounts of oily substances for prolonged periods of time, peritoneal irritation, and retention cysts are the aftermath of such excessive intrauterine and intraperitoneal injections. As shown in a previous study,[4] injections of 8 to 12 c.c. of iodized oil are not only unnecessary but, in addition, they are traumatic and serve as an insult to the peritoneum.

Summary

A method of estimating the potential capacity of the human uterine cavity and Fallopian tubes is described, based on a fluoroscopic study of the quantity of radiopaque oil required to fill these organs in the nulliparous woman.

The average capacity of the normal uterus observed by the writer in 739 cases was 1.7 c.c. of oil, while the Fallopian tubes required an additional 1.0 to 1.5 c.c. of oil to outline the uterotubal tract completely. The inadvisability is pointed out of injecting excessive amounts of viscous radiopaque substance (8 to 12 c.c.) into the uterus for ordinary hysterosalpingographic procedures.

Realization that the uterine cavity of the virgin woman in its nongravid state is actually not a true cavity, but merely a potential slitlike space, should be of practical value in performing uterotubal tests.

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1160 FIFTH AVENUE.

Special Article

ONE THOUSAND CONSECUTIVE DELIVERIES UNDER A TRAINING FOR CHILDBIRTH PROGRAM

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THE following report is based on 1,000 consecutive deliveries (infants 1,500 grams or over) on the University Service of the Grace-New Haven Community Hospital from Jan. 1, 1949, to March 31, 1950. All women were exposed to the Training for Childbirth Program, consisting of educational features both physical and psychological. Our interest in this development in modern maternity care began some four years ago as a result of the writings of Helen Heardman, Grantly Dick Read, Blackwell Sawyer, Edmund Jacobson, and others. Since that time various reports on our experience have come from this clinic, to which reference is here appended.[1-7]

At the beginning of our program we were fortunate in having a visit to our clinic from Mrs. Helen Heardman, who spent some time with us teaching our nurses and physicians exercise techniques which are now incorporated in our procedure. During the first two years we also received material aid from the Maternity Center Association, of New York City, in the form of nursing and medical fellowships. The experience of this organization in the conducting of antenatal mothers' classes represents a pioneering effort in this country.

As our program has developed we have made changes from time to time, which we believe is a sign of healthy growth. In essence the program emphasizes that childbirth is a natural, normal process of the body and that it is important that the prospective mother recognize more fully that bringing a child into the world is a co-operative endeavor in which she plays the most important role. This approach also represents an attempt by physicians and nurses to gain a further understanding of the physiology of childbirth, particularly in its emotional aspects, so that their assistance during the birth process can be intelligently applied. To carry out these aims we attempt to prepare women for childbirth psychologically and physically by means of a training program in which they are taught the fundamentals of reproductive anatomy and physiology and, also, are trained in relaxation techniques and muscle control to aid the natural forces of labor. In labor they are encouraged to use this knowledge and training by those who are in attendance. The conduct of labor and delivery without analgesia or anesthesia is definitely not our primary aim. Our interest is rather directed toward assuring each woman a psychologically and emotionally satisfying labor experience, and one which is at the same time physically safe for both mother and child. We believe that a conscious delivery can be the source of a great sense of achievement for most women—and that in a normal labor, properly conducted, in a woman who has been prepared for the experience, much of the unnecessary pain, which is usually experienced, can be prevented. As the result, small amounts of medication suffice. We do not contend that relaxation alone will prevent all pain—

even in most women—nor that pain is in any sense a desirable or beneficial part of the childbearing experience. For episiotomy and perineal repair we routinely use 2 per cent Novocaine infiltration, seldom finding it necessary to do pudendal block. Our indications for forceps are those generally accepted and we prefer low spinal anesthesia for most instances of such procedure.

The educational aspect of our program consists of four talks given to prospective parents and four exercise classes given by a nurse. In these latter, in addition to training in relaxation techniques, breathing, and postural exercises, the nurse gives instruction in various aspects of pregnancy and labor. Group discussion is encouraged. Following the fourth class, which is given in the third trimester of pregnancy, the women visit the obstetrical division of the hospital, meet members of the personnel, see the labor and delivery rooms, and learn how the delivery tables and anesthesia apparatus operate. Between classes patients practice the exercises at home.

In the four talks to prospective parents the subjects of pregnancy, labor, the newborn, and parenthood are discussed in order. These talks are given by members of the obstetric, pediatric, and psychiatric medical staffs. They are given in the evening during four successive weeks four times during the year, being so arranged that couples will attend the first talk early in pregnancy and the last three during the last trimester. These talks have been quite popular and interesting discussion periods always follow.

In arranging this educational program we have endeavored to satisfy certain needs and at the same time keep the program within reasonable time assignments as far as the professional staff is concerned.

We recognize that "support" during active labor is the most important single factor in our program. Much depends not only on the sympathy and interest of those in attendance, but upon a true understanding of the reasons for and details of the educational program. The satisfaction to be gained from the program is predicated naturally on normal labor in a healthy woman in whom there is no cephalopelvic disproportion, no abnormal fetal position, in whom the soft parts are normally dilatable, the uterine contractions of proper regularity and of suitable force, and the patient deliverable without undue strain on her part. In such "support" we follow several principles. The patient in labor is in a room by herself; during this period she may have her husband with her if she wishes. The patient is kept informed of her progress and during active labor is not allowed to be alone. Attention is focused on her needs and what she is trying to accomplish. Any therapy or instruction is in the hands of a nurse or a physician. Activity and busyness on the part of those attending her are kept to a minimum. Removal to the delivery room is deliberately timed so that plenty of time is available for her preparation.

Before reviewing our results, a word should be said about rooming-in. We feel that the availability of the rooming-in arrangement, whereby mothers and their infants can be together, is an important part of our program. This arrangement is offered to those who desire it. At the present time our facilities (8 beds) are limited and are always oversubscribed. To those interested in further details of both the training program and the rooming-in arrangement, reference is given.[8]

<div align="center">

RESULTS IN 1,000 CONSECUTIVE DELIVERIES
Jan. 1, 1949, to March 31, 1950

TOTAL NUMBER

1,000 women delivered
1,014 infants (birth weight 1,500 grams or over)
86 infants weighed between 1,500 and 2,500 grams
12 twin deliveries
1 triplet delivery

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CLINIC STATUS (UNIVERSITY SERVICE)

Ward	779
Residents' Clinic	130
Private Staff	91

TYPE DELIVERY

(In multiple birth, if one child was delivered operatively, delivery is listed as operative.)

	TOTAL		PRIMIPARAS	MULTIPARAS
Spontaneous	881	(88.1 per cent)	292	589
Operative, total	119	(11.9 per cent)	83	36
Vaginal, operative	78	(7.8 per cent)	60	18
Cesarean section	41	(4.1 per cent)	23	18
Total	1,000		375	625

PARITY

Primiparas	375
Multiparas	625
Total	1,000

ANALGESIA
(DRUG MEDICATION)

	NO MEDI-CATION	PER CENT	DOS-AGE 1*	PER CENT	DOS-AGE 2*	PER CENT	DOS-AGE 3*	PER CENT
Primiparas.—								
352 Vaginal, total	67	19.0	176	50.0	58	16.5	51	14.5
292 Spontaneous	58	19.9	156	53.4	44	15.0	34	11.6
60 Operative	9	15.0	20	33.3	14	23.3	17	28.3

Thus in 214, or 73.3 per cent, of spontaneous primiparous deliveries, not over 125 mg. of Demerol, or 1 dose of another agent, was used. No analgesic was received in 19.9 per cent.

	NO MEDI-CATION	PER CENT	DOS-AGE 1*	PER CENT	DOS-AGE 2*	PER CENT	DOS-AGE 3*	PER CENT
Multiparas.—								
607 Vaginal, total	291	47.9	251	41.4	48	7.9	17	2.8
589 Spontaneous	289	49.0	241	40.9	46	7.8	13	2.2
18 Operative	2	11.1	10	55.5	2	11.1	4	22.2

Thus in 530, or 89.9 per cent, of spontaneous multiparous deliveries, not over 125 mg. of Demerol, or 1 dose of another agent was used. No analgesic was received in 49 per cent.

ANESTHESIA
(INHALATION OR CONDUCTION BLOCK OTHER THAN LOCAL INFILTRATION FOR EPISIOTOMY)

	NO ANES-THESIA	PER CENT	DOS-AGE 1†	PER CENT	DOS-AGE 2†	PER CENT	DOS-AGE 3†	PER CENT
Primiparas.—								
352 Vaginal, total	109	30.9	187	53.1	9	2.6	47	13.4
292 Spontaneous	103	35.2	174	59.6	7	2.4	8	2.7
60 Operative	6	10.0	13	21.7	2	3.3	39	65.0

Thus in 277, or 94.8 per cent, of spontaneous primiparous deliveries, nothing greater than N₂O with contractions was used. No anesthesia was received in 35.2 per cent.

	NO ANES-THESIA	PER CENT	DOS-AGE 1†	PER CENT	DOS-AGE 2†	PER CENT	DOS-AGE 3†	PER CENT
Multiparas.—								
607 Vaginal, total	274	45.1	299	49.3	17	2.8	17	2.8
289 Spontaneous	273	46.3	296	50.3	15	2.5	5	0.8
18 Operative	1	5.5	3	16.7	2	11.1	12	66.6

Thus in 569, or 96.6 per cent, of spontaneous multiparous deliveries, nothing greater than N₂O with contractions was used. No anesthesia was received in 46.3 per cent.

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*1. Not over 125 mg. Demerol or 1 dose of another agent.
 2. 1 dose of 2 agents or 2 doses of 1 agent; if Demerol, over 125 mg.
 3. Greater than 2.

†1. Intermittent N₂O with contraction only.
 2. Continuous N₂O with patient conscious at delivery, or pudendal block.
 3. Spinal anesthesia, or general anesthesia greater than 2.

EPISIOTOMIES
(LOCAL INFILTRATION USED WHEN OTHER ANESTHESIA IS NOT USED OR IS INADEQUATE)

	NO. CASES	INCIDENCE OF EPISIOTOMY	PER CENT
Primiparas.—			
Spontaneous	292	249	85.3
Operative	60	57	95.0
Vaginal total	352	306	86.9
Multiparas.—			
Spontaneous	589	125	21.2
Operative	18	8	44.4
Vaginal total	607	133	21.9

LENGTH OF LABOR
(FIRST STAGE IN HOURS; SECOND AND THIRD STAGES IN MINUTES)

	SPONTANEOUS		OPERATIVE		TOTAL	
	MEAN (AVERAGE)	MEDIAN	MEAN (AVERAGE)	MEDIAN	MEAN (AVERAGE)	MEDIAN
Primiparas.—						
First stage (hours)	11.96	9.4	19.2	12.2	13.2	10.1
Second stage (min.)	51.2	44.0	94.8	86.0	58.6	47.6
Third stage (min.)	9.5	7.4	11.25	8.0	9.8	7.5

(Total length of labor, mean [average], 14.3 hours, median, 11.0 hours)

Multiparas.—						
First stage (hours)	7.3	6.5	13.0	8.3	7.5	6.6
Second stage (min.)	19.71	14.4	79.3	62.0	21.48	14.6
Third stage (min.)	9.71	7.4	9.72	8.5	9.71	7.5

(Total length of labor, mean [average], 8.0 hours, median, 6.96 hours)
Average length of total labor, both primiparas and multiparas, 10.3 hours

RESULTS FOR THE INFANT

Spontaneous Deliveries, 881

In all but 30 the infant's condition was listed as good or excellent on delivery. Of the 30 listed as in fair or poor condition or dead:

4 antepartal deaths
1 intrapartal death (Case A)
3 neonatal deaths, i.e., in first 5-7 days
Cases: E (RH); F (cardiac anomaly?); G (cardiac anomaly)

The remaining 22 all showed improvement in condition during stay in hospital and were discharged in good condition.

Vaginal Operative Deliveries, 78

Six babies not listed as in excellent or good condition. Of the 6 listed as in fair or poor condition or dead:

3 intrapartal deaths (Cases B, C, D)

The remaining 3 improved during stay in hospital and were discharged in good condition.

Cesarean Sections, 41

One fetal death (Case H)—neonatal.

INFANT DEATHS

Antepartal Infant Deaths, 4 (All delivered spontaneously)
Intrapartal Deaths, 4 (Spontaneous 1, operative 3)

Spontaneous delivery, 1

CASE A.—Prematurely ruptured membranes, uterine inertia, medical induction, prolonged labor. Dosage 3 analgesia; dosage 1 anesthesia.

Operative deliveries, 3

CASE B.—Pre-eclampsia, uterine inertia, manual dilatation of cervix, prolonged labor. Midforceps. Dosage 3 analgesia; dosage 3 anesthesia.

CASE C.—Midforceps, oversize baby. Impacted shoulders. Weight 4,920 grams. Dosage 1 analgesia; dosage 3 anesthesia.

CASE D.—Compound presentation, prolapsed arm, version and extraction, 4,245 grams. Dosage 1 analgesia; dosage 3 anesthesia.

Neonatal Deaths, 4 during stay in hospital (usually 5 to 7 days)

After spontaneous deliveries, 3

CASE E.—In child with marked signs of erythroblastosis fetalis delivered by Rh-negative woman (originally reported to be Rh positive). Condition poor on delivery, died 10 minutes later.

CASE F.—Spontaneous delivery after 6¼ hours' labor of para i, gravida ii, abortus 0 woman. Weight 3,240 grams. Condition good on delivery, died in 2 hours. Believed by pediatricians to have cardiac anomaly but post-mortem examination refused by parents.

CASE G.—Spontaneous delivery after 3½ hours' labor of a gravida x, para viii, abortus i woman. No analgesia; dosage 1 anesthesia. Weight 3,900 grams. Died on sixth day. Congenital heart defect. Transposition of aorta and pulmonary artery demonstrated at autopsy.

After cesarean section, 1.

CASE H.—For placenta previa. Fetus became apneic and died 26 hours after delivery. Cause unknown. No post-mortem examination allowed.

In conclusion we believe the results which are shown here statistically are worthy of consideration. The loss of 8 infants intrapartally and neonatally (1,500 grams or over), 0.8 per cent, in 1,000 consecutive deliveries is a low figure. In three of these, E, F, and G, it is doubtful if any different obstetrical procedure would have changed the result. We do not ascribe this low fetal loss directly to the training program. Nevertheless, we believe that the minimal amounts of anesthetic agents used and the relatively shortened duration of labor do favor such a result. We recognize that comparison with work done in other clinics is difficult because many factors enter into such reports. We are thinking of such factors as type of clinical material, incidence of hospital delivery in the area, incidence of neglected cases sent to the hospital for delivery, adequacy of antenatal care outside the clinic. In addition, however, to what might be called the safety factors, as shown by the above analysis of our results, we consider that there are important values in our program which are not subject to such methods of appraisal. We refer to the values of education for maternity, so ably emphasized by Dean McIntosh at the International and Fourth American Congress on Obstetrics and Gynecology, who said, "The skill and experience of the doctor and the man of science should in some way be interpreted more clearly to the layman, through greater understanding and closer co-operation between the teacher and the physician, and of both with the individual. . . . If physicians and educators work together, they will recognize that preparation for maternity is the most important task of our society."

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Department of Case Reports
New Instruments, Etc.

PREGNANCY COMPLICATED BY PARTIAL BOWEL OBSTRUCTION AND CONVULSIVE TOXEMIA

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PREGNANCY complicated by bowel obstruction is unusual, more so when pregnancy is complicated by bowel obstruction and convulsive toxemia of pregnancy. A happy outcome for the mother and child despite these serious complications makes us feel that this case is worth reporting.

Mrs. T. B. was first seen in consultation following admission to Sibley Hospital with nausea and vomiting which had persisted for several days prior to admission. The history revealed a long period of chronic indigestion, an appendectomy twelve years previously, and continuous intermittent retching and vomiting throughout her present pregnancy which was in the seventh month at the time of the consultation. Physical examination revealed an asthenic 26-year-old white woman in great distress. She was quite dehydrated, with a foul breath and dry sallow skin. The abdomen was enlarged by a seven months' pregnancy and a superimposed marked intestinal distention. Her pain was general without localized tenderness or rigidity. There was tympany on percussion, but normal peristalsis was present. The impression was of an existing pylorospasm or cardiospasm with a possible bowel obstruction to be ruled out. A gastrointestinal series demonstrated no other gastrointestinal abnormality than a large amount of gas throughout the entire tract. This was felt to be suggestive of a partial bowel obstruction.

Supportive measures were instituted. Over a period of a few days much of the vomiting and retching were relieved and the distention overcome. Operative intervention was not felt necessary at this time, since it was believed the patient might have resolved the partial obstruction spontaneously. Hence she was discharged as clinically improved.

Ten days following her previous admission and about two days after discharge she was readmitted markedly distended with moderately severe dehydration. Loops of bowel could be identified easily through the thin abdominal wall. It was felt that though the obstruction was still partial it was incapable of spontaneous resolution; accordingly, surgical consultation was had. As a result Miller-Abbott tube and Wangensteen suction drainage were instituted to reduce the distention and locate more exactly the point of obstruction. Repeat x-rays of the abdomen served only to substantiate the diagnosis of partial obstruction. Suction drainage was continued while the patient was sustained on almost continuous intravenous fluids, since all attempts at oral feeding resulted in increasing distention. Finally, after occasional temporary improvement, it became obvious that operation was indicated. A right rectus incision was made with exploration of the distended bowel. A band of adhesions between the ileum and cecum was found. A loop of ileum was incarcerated between two portions of the bowel and the adhesion. Lysis

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of the adhesions was done and the bowel freed. The Miller-Abbott tube was found to be at the head of the ileum and was milked down to the area of edema and incarceration. Further exploration revealed no other abnormalities. The postoperative course was one of steady improvement for the first seventy-two hours, but on the fourth postoperative day she suddenly complained of blindness. She began to convulse rapidly with an initial tonic stage followed by gross twitchings of the face, arms, and legs. The clonic phase was followed by a period of coma. This recurred five times in fairly rapid succession. Pentothal Sodium was given intravenously and the convulsions ceased. The blood pressure which had been about 140/85 since admission was recorded as 190/60. Hypertonic glucose and magnesium sulfate were administered intravenously together with morphine. Abdominal examination several hours following the convulsions revealed rhythmic uterine contractions. Rectal examination showed the cervix to be effacing and partially dilated. The membranes were ruptured artificially and under low spinal anesthesia a normal living 4 pound, 8 ounce female infant was delivered by prophylactic low forceps after ten hours of labor. The condition of mother and child was good. Following delivery, the patient was given a transfusion of 500 c.c. citrated whole blood. Her blood pressure was 160/90. The following day, despite an apparent definite improvement in her condition, she had two more convulsions. These were controlled by rectal paraldehyde. The patient remained well sedated, her blood pressure was 120/90, and she had no further convulsions. Except for complaints of severe headaches and an occasional abdominal cramp she seemed much improved in the next twenty-four hours. She voided easily and frequently, the bowels functioned well, her appetite increased rapidly. Finally, twelve days after her operation and eight days post partum, she was discharged. When she was seen five weeks post partum, her blood pressure was 120/70, the pelvic organs were perfectly normal, and except for some asthenia she was fully recovered. Her last examination was made less than a year ago nearly three years after her operation and at that time she was well and free of complaints.

Comment.—This case is interesting not only because of its rarity but also because it shows how the treatment of one complication may be a precipitating factor in another. During the period of acute bowel obstruction the patient was sustained on intravenous fluids, among them many containing saline. It has been a question in our minds as to whether our attempts at balancing chloride loss through the Wangensteen drainage were not in reality the precipitating factor in the causation of the eclampsia.

ARRHENOBLASTOMA OF THE OVARY

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(From the Department of Obstetrics and Gynecology, Mount Sinai Hospital)

J C., an unmarried white woman, aged 21 years, was first seen in December, 1949, complaining of secondary amenorrhea of two years' duration. Her menarche had been at 12 years of age, succeeding periods being regular each month with a five-day flow, normal in character but accompanied by marked dysmenorrhea. Following a customary period in early December, 1947, the patient developed sudden and complete amenorrhea except for two days of slight staining in April, 1948. There was no cyclic discomfort or pain after the cessation of the menses.

The patient noticed that in a short time her breasts became considerably smaller. This was followed by the loss of normal female hip contour; the patient noticed her clothing no longer fitted properly. Six months later, she was aware of an increase in size and sensitivity of the clitoris, so much so, that it was continually irritated by her clothing. During the second year of amenorrhea she developed an increasing quantity of hair about the face, between the breasts, and around the nipples. In a short while, it was necessary for the patient to shave.

There were no skin discolorations and no known hypertension. Her weight remained constant. The patient was herself aware of a personality change, developing a marked moodiness which, on questioning, she frankly attributed to self-pity because of hirsutism.

Physical examination revealed an alert, intelligent girl with hirsutism of the face and chest. Her voice was definitely feminine in character, and the skin white and clear. The breasts were very small, the hips flat, and a male type escutcheon was exhibited.

The blood pressure was 118/76, the lungs clear, and the heart normal. There were no palpable abdominal masses. The clitoris was erect and enlarged, measuring approximately 4 cm. The hymen was intact, and the remainder of the external genitals were apparently normal. Rectal examination revealed a small, firm uterus in mid-position, to the right of and behind which was felt a firm, egg-sized mass. A clinical diagnosis of arrhenoblastoma was made.

The patient was operated upon Dec. 31, 1949. A solid tumor of the right ovary and a "chocolate cyst" of the left ovary were found. The operative procedure consisted of a right salpingo-oophorectomy, partial resection of the left ovary, and prophylactic appendectomy. The patient's postoperative course was entirely uncomplicated.

Twenty-eight days postoperatively the patient had her first period which was scant. The second period appeared exactly twenty-eight days after the first and was the same as those which preceded the amenorrhea. Neither of the two periods was accompanied by dysmenorrhea.

Examination two and one-half months after operation revealed that the breasts had filled out and that the subcutaneous buttock and hip fat had returned. The hirsutism had markedly decreased, with but a slight fuzz remaining on the upper lip and some hair around the nipples. The clitoris was still large but was soft and flaccid, being neither tender nor irritable. The patient's mental outlook was markedly improved.

Pathologic Report (Dr. David R. Meranze).—

Macroscopic: The specimen consisted of a rounded, circumscribed mass measuring 5.5 by 4 by 3 cm. The surface was smooth, glistening, and contained a small adhesion, and several cysts measuring 3 mm. in diameter. At one pole, there was a roughened area from

which several blood vessels projected. On section, there was revealed an outer shell of gray-white, firm tissue which varied from 1 to 4 mm. in thickness and contained several tiny cysts. There was a central, circumscribed, encapsulated, solid, grayish-orange mass which filled the remainder of the specimen. The cut surface of this central area was relatively homogeneous. No cystic areas were seen.

Microscopic: Sections of the ovarian mass revealed a thin shell of compressed ovarian stroma surrounding a well-demarcated, neoplastic mass. This was composed of irregular collections of large, dark spindle cells separated by fibrous septa. These cell groups ran in various directions, imparting a whorled appearance. An occasional cell was larger than others. Rarely, the cells were grouped to form acini. Intermingled with these elements were small groups of larger, pale, polygonal cells with rounded, vesicular nuclei. The neoplasm appeared to be an arrhenoblastoma of the sarcomatous type, with only the slightest suggestion of small tubules here and there. Collections of Leydig-like cells were fairly prominent throughout the neoplasm, and accepted lipoid stains with special techniques.
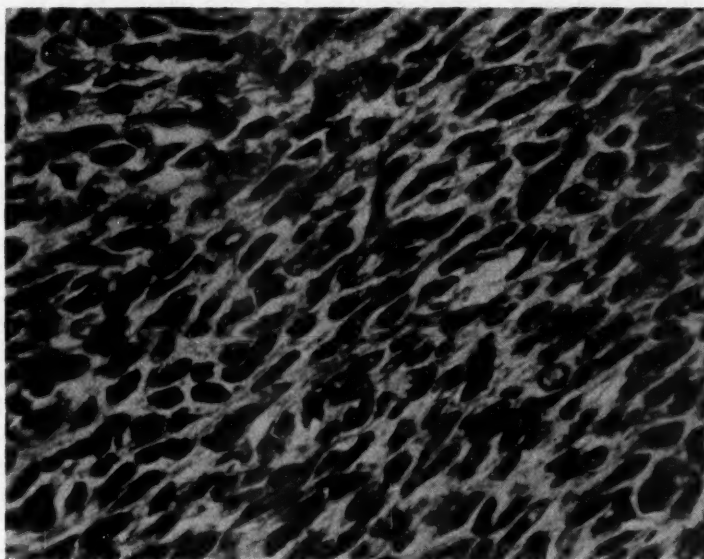

Fig. 1.—Arrhenoblastoma of the ovary of the highly undifferentiated sarcoma-like type.

The histologic preparations were reviewed by Dr. Emil Novak who agreed that the tumor represented an arrhenoblastoma of the highly undifferentiated, sarcoma-like type (Fig. 1). He cautioned, however, that, although the prognosis in a tumor of this type would be reasonably good, the possibility of recurrence must ever be borne in mind. Experience so far has shown a 25 to 30 per cent recurrence in such cases.

The case here presented is typical. It appeared *suddenly* in a young, unmarried woman. It manifested itself by amenorrhea, loss of breast contour, decrease of girdle fat, hirsutism, and by clitoral enlargement.

As is reported in other cases of arrhenoblastoma, the determination of the urinary 17-ketosteroids was of no diagnostic or prognostic value. The preoperative level in the 24-hour-urine specimen was 10.4 mg., and, in the postoperative specimen, 9.3 mg. The normal range for women is 5 to 15 mg. in 24 hours.

Removal of the tumor brought marked improvement with regression of the clinical changes. Although the histologic pattern of the tumor was, in part, almost sarcomatous in nature, it is felt that the age of the patient sanctioned the conservative type of operation performed. It is intended to observe the patient carefully for any evidence of recurrence or sign of malignancy.

CARCINOMA OF THE CERVIX SIMULATING PLACENTA PREVIA

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A 33-YEAR-OLD white married woman, gravida viii, para vii, was admitted on Nov. 11, 1948, one week from term, complaining of painless vaginal bleeding of three hours' duration. She was not in labor.

She stated that she had been awakened during the night by the passage of a large clot of blood followed by a slight trickle of bleeding which persisted until entry. She had no prenatal care and stated that there had been no vaginal spotting or bleeding prior to the onset of the present episode. Previous pregnancies, labors, and deliveries were uncomplicated. Her oldest child was 13 years of age and her youngest 14 months old. Her longest labor was of seven hours' duration. Her menstrual periods were normal between pregnancies, and her medical and surgical history was not significant.

The temperature, pulse, and respirations were normal. The blood pressure was 135/80, red cell count 3.5 million, hemoglobin 11.0 Gm. per 100 c.c. The uterus was enlarged to the size of a term pregnancy. The fetal heart rate was 132 heard in the left lower quadrant. The head was dipping into the pelvis. Rectal examination was not done. Direct placentography showed the placental shadow to be on the right lateral uterine wall. A tentative diagnosis of marginal placenta previa was made, and whole blood was obtained. Bleeding subsided shortly after the patient was put to bed, and vaginal examination was not done. Ten hours following admission the patient began having painful uterine contractions, and, after two hours of labor, delivered spontaneously a normal male infant. There was no perineal laceration. The placenta was delivered intact without marginal fraying. The blood loss was recorded as 150 c.c. Bleeding following delivery was not excessive, and the patient left the hospital on the third postpartum day, against the advice of the staff. She did not return for postpartum examination.

Eight months following delivery she came to the clinic complaining of vaginal bleeding which had gradually increased in amount since the birth of her baby. Pelvic examination revealed an exophytic growth which involved the entire cervix. There was extension into the right fornix. Histological examination of tissue obtained by biopsy showed squamous-cell carcinoma of the cervix.

Comment

It is reasonable to assume that, in this case, the vaginal bleeding which occurred prior to delivery was caused by the carcinoma of the cervix. Although cervical carcinoma is only rarely the etiological factor in vaginal bleeding during pregnancy, it should be considered. Vaginal examination should be done in all cases where the facilities for definitive treatment of bleeding in the last trimester are available.

MALIGNANT TERATOMA OF THE OVARY IN ADOLESCENCE

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THE occurrence of teratomas in the first two decades of life is rare. The literature[1] has recently been reviewed and only 150 cases were found. Since then, no further cases have been reported. Because of the rarity of these tumors and their tendency toward malignancy, the following case appears worthy of record.

The patient (Chart No. 1262), a 16-year-old nulliparous Negro girl, admitted to the Gynecological Division of City Hospital, complained solely of rapid abdominal enlargement. This symptom had been present for six months but became more noticeable in the last two months.

Physical examination revealed a well-developed, obese Negro girl with strong android habitus and marked hirsutism of the face and chin. A nontender tumor mass was found, emanating from the pelvis, reaching the xiphoid, and extending to the flanks. The introitus was nulliparous and the clitoris was slightly hypertrophied. On bimanual examination, the tumor was immobile, doughy in consistency, and filled the entire pelvis. The uterus could not be distinguished. The cervix was flush with the vaginal vault and the os was closed.

Roentgenological examination of the abdomen revealed a sharply demarcated mass obscuring the entire left side from the pelvis to the diaphragm. Its appearance was strongly suggestive of encapsulated fluid. No fetal parts were demonstrated.

The temperature, pulse, respirations, blood pressure, hemoglobin and urine were normal. The Friedman test for pregnancy was negative. A preoperative diagnosis of giant ovarian neoplasm was made.

At operation, an ovarian mass the size of a full-term gravidity with both solid and cystic areas was found arising from the right adnexa. It filled the entire pelvis and abdomen and encroached upon the diaphragm. The right tube was edematous, flattened, and firmly adherent. The left ovary was three times normal size and contained a hemorrhagic corpus luteum cyst. The left tube was normal. The uterus was wedged against the symphysis by the tumor and was normal in size. Because of the extreme immobility of the mass, a trochar was inserted into the cystic portion and approximately 1,200 c.c. of glairy, blood-tinged, straw-colored fluid were drawn off. The mass was then mobilized and a supracervical hysterectomy and bilateral salpingo-oophorectomy were performed. The abdomen was closed in layers following the three-string technique employed on this service.

The postoperative course was uneventful and the patient was referred to the clinic on the seventh postoperative day. Two months later there was no evidence of recurrence or metastasis.

Pathologic Examination.—The specimen consisted of a supracervically amputated uterus and both adnexa. The right ovary was replaced by a large ovoid mass, measuring 25 by 15 by 10 cm. The superficial veins were prominent. The outer surface was smooth. There was one large collapsed cyst and a large solid area. On section the solid area had many small cysts filled with clear fluid, blood-stained fluid, or sebaceous material. In the solid foci, adipose tissue, hair, skin, bone, and teeth were recognizable.

The right ovary had a hemorrhagic corpus luteum. The uterus and tubes appeared normal.

Microscopic Examination.—A great variety of tissue was found, usually adult, occasionally embryonal. The systems most frequently represented were the nervous, respiratory, and cutaneous. Glial tissue was very abundant and was mainly adult in type. However, there were some foci of embryonal nature. Ependyma was well represented as was the choroid plexus. There were some areas resembling cortex with neuronal cells. Some nests of piarachnoid had melanin-bearing cells. There were well-formed nerves and ganglia. Respiratory epithelium was very abundant and always adult. Complete bronchial structures were represented with mucosa, submucosa, seromucous glands, fibrocartilage, and involuntary-muscle bundles. Small bronchi were present in scanty numbers. There were junction points of respiratory and squamous epithelium and glandlike structures lined by respiratory epithelium with squamous nests. The skin had the accessory structures of hair, sebaceous glands, and a few sweat glands. Many foci had embryonal hair shafts.

Other systems were represented in lesser degree. There was gastric mucosa, one focus showing junction with squamous epithelium strongly suggestive of cardia. Salivary gland structures were fairly numerous. There was a focus of large bowel type, and one resembling small bowel. There was a structure similar to Fallopian tube with the two types of epithelial cells.

Adipose tissue was abundant and had foci of embryonal fat cells. The fibrous tissue varied in cellularity, some foci were extremely cellular, although not embryonal in character. There were nests of melanophores. There was well-formed cartilage, developing and adult bone, and small nests of voluntary muscle. Involuntary muscle was abundant. The other organs were normal.

Diagnosis.—Malignant teratoma of right ovary.

Comment.—Most of the tissue was adult in nature and none had the histological criteria of malignancy. However, the embryonal nature of the glial tissue, especially, strongly supports the diagnosis of malignancy and corresponds to observations made in reported cases. The presence of the very cellular fibrous tissue and the embryonal nature of the cutaneous accessory organs and fat add further support to this conclusion. These features apply particularly to the age period of the patient. The prognosis is poor or, at best, very guarded.

Reference

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RADIOACTIVE IODINE FOR HYPERTHYROIDISM ADMINISTERED DURING EARLY PREGNANCY

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WITH the advent of the use of radioactive substances for the treatment of various diseases, a new factor has been introduced which might adversely influence the developmental process of the fetus.

The following is a report of the use of radioactive iodine for the treatment of hyperthyroidism administered during early pregnancy before the existence of the latter had been discovered.

Case No. 3256. A 42-year-old white woman was first seen July 22, 1949, presenting herself because she believed she was pregnant. She had had one other pregnancy sixteen years previously. Significant past medical history concerned itself with the thyroid gland. In 1946 the patient had a thyroidectomy for hyperthyroidism. At this time her basal metabolic rate was plus 30; there had been a rapid weight loss to 89 pounds; there was marked nervousness with an increase in size of the thyroid gland. The pathologic diagnosis on the subtotally excised gland had been "adenomatous goiter and chronic thyroiditis."

In January, 1949, the patient had a course of thiouracil over a three-day period for recurrent hyperthyroidism. This was poorly tolerated, and therefore discontinued, and had little clinical effect.

On April 26, 1949, the patient received 5 mc. of I 131 for the persisting hyperthyroidism. The Cleveland Clinic reported at this time a slight exophthalmus, a small amount of tissue palpable high on the left, weight 100 pounds, B.M.R. +32, and an uptake of the radioactive iodine of 70 per cent.

At the time of the administration of the I 131, the patient was ten weeks amenorrheic, her last menstrual period having been Feb. 15, 1949. Periods had been regular and fairly normal.

Subsequent to the treatment the patient began to notice a definite improvement in toxic symptoms. She was less nervous and had gained weight. She continued amenorrheic. She suspected pregnancy just prior to her first visit when her abdomen began to enlarge even out of proportion to her general weight gain and she believed she felt fetal movements.

On examination it was found that the patient was five months pregnant; fetal heart sounds were heard and general physical and pelvic examinations were otherwise negative except for the presence of several small uterine fibroids and a marked paleness of the mucosa and skin. Red corpuscle count was 3.2 million, cells showed hypochromia; the patient's weight was 120 pounds.

During the subsequent antepartum visits the patient's progress was uneventful except that she was persistently "tired." B.M.R. was checked at +3 on Aug. 9, 1949. Weight gain was to 135 pounds.

On Nov. 11, 1949, the patient was delivered by low forceps of a male infant weighing 5 pounds, 12 ounces under saddle block anesthesia after a labor characterized by moderate primary uterine inertia.

The postpartum course was uneventful. Basal metabolic rate was reported as +3.

The infant, although appearing slightly immature, evidenced no physical findings of note. He appeared vigorous, took formula well, and was discharged at birth weight on the

seventh day following delivery. Dr. Campbell Moses, Chairman of the Radiation Hazard Committee of the University of Pittsburgh Medical School, advised us that he was certain that Geiger counter studies of the mother post partum, or infant, would reveal no activity in the postnatal period so this procedure was not done although the idea was considered. This would have been seven months after administration of the radioactive material.

At six weeks and five months, respectively, following delivery examination of the infant revealed him to be developing normally. Weight at last visit was 13 pounds, appetite was good, he showed a normal emotional response, held his head up, and in every way, physically and developmentally, seemed to be progressing normally.

Comment

This subject presents many interesting aspects.

This patient had received a small dose of radioactive iodine at eight weeks' gestation. Why she chanced to be pregnant at this particular time after sixteen sterile years is questionable. Perhaps the thiouracil induced just enough improvement in the endocrine balance to permit this.

However, the question of main concern and complexity was what influence the atomic therapy would have on the fetus at such a critical stage of development. There are, according to Nickson,[1] four classes or types of damage associated with exposure to radiation, namely, the induction of neoplasms, the production of blood dyscrasias, the production of genetic changes, and the shortening of the span of life.

Many possibilities for the developing fetus seemed to present themselves, such as deaf-mutism, congenital cataract, harelip, or other anomalies similar to the effect of German measles virus during early pregnancy.

The fate of the fetal thyroid in the presence of the possible destructive influence of radioactive iodine was of major concern. Failure of development of a functioning thyroid gland in the fetus would undoubtedly result in an athyrotic cretinism. If it was not destroyed, the question arose of whether the gland, in the presence of maternal hypothyroidism, would be stimulated to compensatory overproduction or hypertrophy such as occurs with the pancreas of the infant of a diabetic. Would delivery precipitate a thyroid crisis or something less in the infant? These and other questions arose to cause us concern with only a few facts to turn to in recorded literature.

Chapman and his co-workers[2] analyzed the thyroid tissue by Geiger counter in nine fetuses ranging in age from 7 to 32 weeks, whose mothers were about to have therapeutic abortion for some type of organic disease and were given tracer doses of radioactive iodine experimentally before the operation. They concluded that the human fetal thyroid does not take up radioactive iodine in the first twelve weeks of life but that after the fourteenth week increasing amounts are taken up.

Hertz,[3] of Boston, in a recent personal communication, stated that his group has treated a series of 189 hyperthyroid patients with radioactive iodine. In this group 16 pregnancies subsequently resulted to 11 mothers and 3 fathers who had been so treated. None of these 16 infants showed cretinism or any other congenital defects. He has not, to his knowledge, treated anyone during pregnancy, but two cases in which the stages of gestation were not given have been reported to him in Boston. These were the ones mentioned in the article by Chapman and co-workers,[2] referred to previously. Both infants have been apparently normal. Hertz adds that the normal thyroid is relatively resistant to radiation and he believes it is even safe deliberately to treat patients who are known to be pregnant, depending upon the selectivity of the mother's toxic thyroid for removal of the radioactive iodine without fear of damaging the fetal thyroid in any way.

Crile[4] also in a communication stated that he believes that this material can be used with perfect safety up to the fourth month of pregnancy but his group has not knowingly used it. In respect to the possibilities of damage to the fetus in the early months of pregnancy, he further stated that he believes one need have little concern because the thyroid

has the ability of concentrating radioactive iodine by a factor of 10,000 to 1 as compared with a concentration of the element in the blood and other tissues of the body and that, therefore, the maternal thyroid receives approximately 10,000 times as much radiation as does the fetus.

This single case appears to have had a fortunate outcome thus far, but it would seem inadvisable to use atomic elements during pregnancy for fear of inducing a miscarriage or some anomalous genetic change even if the dosage were small.

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3. Hertz, Saul: Personal communication.
4. Crile, George, Jr.: Personal communication.

MULTIPLE ARTERIAL THROMBOSES IN A NEWBORN INFANT, WITH PARTICULAR INVOLVEMENT OF AN UMBILICAL AND HYPOGASTRIC ARTERY

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(From the Department of Laboratories, Beth Israel Hospital)

MILLS[1] reported under the title, "New Neonatal Syndrome," eight cases characterized by circulatory disturbances involving predominantly the lower limbs. These cases were seen during a period of ten months. He was able to find one similar case in the hospital records of the previous year; he had not seen any thereafter. "The chief characteristics include the onset of vascular disturbances shortly after birth in one or both lower extremities, with predilection for the gluteal region, and sometimes a flaccid paralysis of the limb. In one infant there was a fatal issue from cerebral hemorrhage; in another the inferior mesenteric vessels were affected and the child died from peritonitis; in a third there was residual paralysis of the anterior tibial group of muscles. All the remainder recovered fully." Mills' study of his eight cases revealed that all of the infants had been in a state of "white asphyxia" at birth and required injection of nikethamide. He suggested that, in the stress of the emergency, the injection had been made into one or both of the umbilical arteries instead of the collapsed umbilical vein.

His report recalled an autopsy performed in this hospital in 1937, and the close correspondence of the history and the autopsy findings to the cases of Mills would appear to warrant its publication.

Male infant F. was born on Sept. 28, 1937; respirations and cry were delayed. One c.c. of Coramine was injected into the umbilical vein (according to the obstetrician's notes), and the infant was treated by immersion in warm water. Nine hours later, he was seen by a pediatrician who found the left leg, from the hip down, a mottled purple. The discoloration involved the scrotum. The anterior abdominal and the gluteal regions were also involved. The left leg was cooler than the right, was flaccid, and was moved to a lesser degree than the right. A few purplish spots were also noted on the right ankle. The cry was shrill; there was a slight tremor of the arms; a convulsion occurred that morning. The next day the discoloration of the left leg was somewhat deeper, though appearing more mottled. It was felt that a thrombosis of the left common iliac artery explained the lesion. The next morning the infant had numerous convulsions. The discoloration of the buttock and, in some areas, of the leg had deepened. Blebs formed in the skin, which appeared necrotic. The child died early that afternoon.

Autopsy was performed 20 hours after death. The postmortem appearance of the left lower limb is shown in Fig. 1. The left umbilical and hypogastric artery was completely occluded by a brown, rather firm, inelastic thrombus, extending from the anterior abdominal wall to the point of junction with the left common iliac artery. A somewhat more red and friable thrombus, not adherent to the wall, extended beyond for a distance of about 5 mm. into the left common iliac artery. At the point of bifurcation of the left common iliac into hypogastric and external iliac, pinhead, firm, gray thrombotic nodules projected into the lumen of the external iliac, partly occluding it. Beyond, this vessel was traced to the popliteal space, and was free of thrombus. The vessels of the right leg were unobstructed. There was no venous thrombosis. Small hemorrhages were found in the cortex of the right adrenal and in the cortex of the right kidney. Microscopically, thromboses of varying age

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Fig. 1.—Post-mortem photograph showing the mottled discoloration of the left lower extremity, extending from the iliac crest to the sole of the foot. The discolored areas were deep purple, of irregular outline, and raised above the general surface. Over the buttock, and over the lateral aspect of the leg, the skin is desquamated over extensive areas.

Fig. 2.—Cross sections of the umbilical arteries immediately within the anterior abdominal wall. The left is occluded and distended by thrombus. (H. and E. ×15.)

Fig. 3.—Thrombosed left umbilical artery, proximal to Fig. 2. Note the thrombus in the small adventitial artery. The occluded urachus is seen at the upper right. (H. and E. ×15.)

Fig. 4.—Thrombosis of left hypogastric artery. (H. & E. ×15.)

Fig. 5.—Thrombus in small pulmonary artery. (Trichrome stain. ×70.)

Fig. 6.—Thrombosis of an interlobular renal artery. (Trichrome stain. ×20.)

Fig. 7.—Thrombosis of small artery adjacent to pancreas. (Trichrome stain. ×20.)

were found in the vessels described as being occluded (Figs. 2 to 4). In addition, thrombi, of some age, were found in small vessels of the lung, thyroid, spleen, pancreas, adrenal, and kidney (Figs. 5 to 7).

At the time of the autopsy, the possible relation of the injection of Coramine to the findings was considered, but this explanation was rejected because it was not possible to relate the distribution and age of the arterial thromboses to an injection into the umbilical vein. The possibility of intra-arterial injection was not considered. Even now, it is difficult to understand how the injection of the drug into an umbilical artery could cause thrombosis in distant small arteries such as those of the lung or pancreas. Too much weight, perhaps, should not be placed on the seemingly older appearance, histologically, of the thrombi in the smaller arteries as compared with those in the major vessels to the left leg.

The full explanation of this group of cases probably must await experimental reproduction of the lesion. Until that time, however, it might be well to accept the explanation of Mills, and take all precautions to obviate intra-arterial injection when an obstetric emergency requires the use of intravenous medication.

Summary

Multiple arterial thrombi in a newborn infant, involving the left umbilical and hypogastric artery, with interference with circulation to the lower limb, gluteal and scrotal regions, and the development of cyanosis, tissue breakdown, and flaccid paralysis, are described.

The similarity to the syndrome recently reported by Mills is pointed out; the widespread vascular involvement in the present case raises doubts as to the validity of the etiological explanation, proposed by Mills, that the injection of nikethamide into an umbilical artery produces arterial thrombosis or spasm, with the consequent effects as described.

Reference

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AN IMPROVED URINAL*

C. O. McCORMICK, M.D., INDIANAPOLIS, IND.

THIS urinal in conjunction with an anchored catheter is advantageously useful during abdominal cesarean sections and those pelvic operations in which an empty bladder is to be maintained. It is made of stainless steel, and has an ample capacity of 10 ounces. Its lateral surfaces conform to the inner surfaces of the patient's thighs, and its narrow
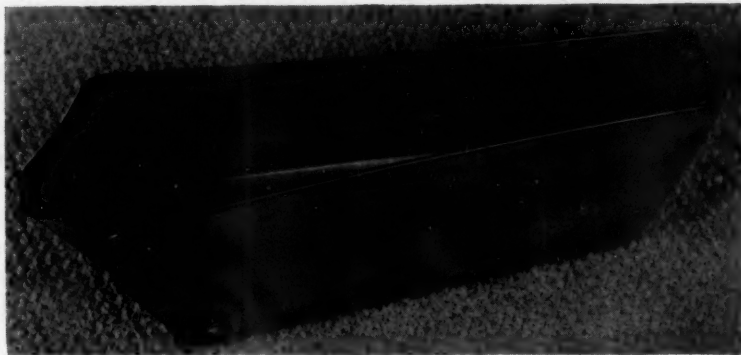

Fig. 1.

transverse diameter (one inch at the top at the narrow end) permits close approximation of the limbs. It is designed to replace the commonly used circular and vomitus basins, both of which allow easy spilling of the urine, and require undesirable separation of the limbs.

621 HUME MANSUR BUILDING

Department of Book Reviews

EDITED BY PHILIP F. WILLIAMS, M.D., PHILADELPHIA, PA.

Review of New Books

Gynecology

Professor Martius' **Operative Gynecology**[1] appears in its sixth edition, the first since 1945. The work has been thoroughly revised and the pertinent new literature included. The basic plan of previous editions remains, however. The anatomy of the region to be considered is first thoroughly discussed, and then the various operative procedures are clearly and completely detailed.

Much of the merit of this book stems from the illustrations, which are both diagrammatic and detailed in type. All are drawings (most of which are colored) of remarkable clarity.

The book includes sections upon gynecologic laparotomies, vaginal procedures, operations for urinary incontinence, curettage of the uterus, herniotomy, and intestinal surgery. The latter two are particularly welcome in a book of this type. The section upon vaginal surgery is especially outstanding.

This sixth is a very worthy successor to previous editions, and an excellent example of modern German books on the subject.   BRUCE A. HARRIS, JR.

Miscellaneous

That the preparation of his biography was anticipated by the late Dr. Joseph B. DeLee is borne out by a careful reading of the volume.[2] The work is a joint effort of Dr. Sol DeLee, his nephew, and Dr. Morris Fishbein, aided by former associates of the elder DeLee, both lay and medical, and is pleasing in its style. Dr. DeLee died April 2, 1942, at the age of 72. From his early days, apparently, he had kept a diary, minute in many details, and touching upon all phases of his busy and many-sided life. Access to such a wealth of facts and data undoubtedly provided the authors of the biography with much detailed information of a substantial character.

The early part of the book refers to DeLee's French and Polish ancestory and gives intimate glimpses of his early life, and the close family solidarity, imbued as it was by the stern discipline of the orthodox Jewish faith. From clerking in a drugstore, DeLee went on to medicine, graduating from the Chicago Medical College in 1891. He early appreciated the excessive toll of childbirth and infant life, and the influence of what he had seen and his desire to improve these dire conditions early became the motive of DeLee's life. Within a few years of graduation, by dint of personal effort and sacrifice, he and sympathetic friends established the Chicago Lying-in Dispensary at Maxwell Street and Newberry Avenue for the systematic care of expectant mothers.

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[1]**Die gynäkologischen Operationen und ihre topographischen-anatomischen Grundlagen.** By Heinrich Martius, M.D., Director of the Göttingen University Woman's Clinic, Göttingen, Germany. Sixth edition. 426 pages. 422 illustrations, mostly colored. Stuttgart, 1950, Georg Thieme Verlag. Price, DM 60.

[2]**Joseph Bolivar DeLee—Crusading Obstetrician.** By Morris Fishbein, M.D., with Sol Theron DeLee, M.D. First edition. 313 pages with frontispiece in color. New York, 1949, E. P. Dutton and Co., Inc. (Printed by the William Byrd Press, Inc., Richmond, Va.)

From this point, the authors trace DeLee's progress in considerable detail, from the first home of the Lying-in Hospital on Ashland Avenue, through the planning stages of a larger and greater hospital during which time his life-long feud with Mrs. Kellog Fairbank began and continued long after the completion of the Mother's Aid Pavilion in 1914. In spite of personal disagreements as to policy, DeLee is quoted as frankly recognizing Mrs. Fairbank's invaluable services in the matters of finance and personal relations, which aided so greatly in eventually bringing to fruition the Vincennes Avenue Buildigs. The successive episodes that culminated in the affiliation of Lying-in with the University of Chicago, and DeLee's fight to retain certain rights and privileges for Northwestern University are explained by the authors as a ''frustration which colored the remainder of his [DeLee's] life,'' even though his loyalty to Lying-in kept him in line with the final move.

The reader will find many entertaining recitals of striking episodes in the life of this many-sided man. Sincere attempts are made to explain his peculiarities of personality and temperament. There is frank exposure of the faults and idiosyncrasies of which his associates were aware. He was philanthropic and socially conscious, but generally aloof; he could be his own worst critic, but seems to have tortured himself unduly. It seems paradoxical that one who early championed hospital residence for obstetric care should have become involved in later life in so unfortunate a controversy in the lay press regarding the superior safety of home delivery when compared with delivery in general hospitals, because of a misunderstanding of DeLee's idealistic interpretation of the subject.

Throughout the entire book, however, runs the underlying theme—that Joseph B. DeLee was a pioneering and controversial obstetrician. Always a perfectionist and well equipped professionally, this outstanding author and teacher takes his rightful place among the outstanding physicians of our time. The book ends in a reverent vein, for Rabbi Mann's final words at his old friend's bier—''Know ye that a prince and a great man has fallen this day in Israel''—were justly true.   LEWIS C. SCHEFFEY.

In the **Principles of Human Genetics**[3] we have available for the first time a comprehensive exposition of the science of genetics based on and applied to man. Genetics is a young science and until the present time writers of books on the subject have found it necessary to base their discussions in large measure on material obtained from experiments on plants, animals, and microorganisms. Dr. Curt Stern in the present volume has succeeded in writing a book entirely about human beings and has found it possible to discuss all phases of genetics in terms of human traits instead of the customary pea blossom and Drosophila. The book can serve the beginning student as an introduction to the general problems of the subject and at the same time afford the advanced student adequate reading material in a specialized field. Its great interest for the medical practitioner will rest in the fact that it deals with human beings and that the situations discussed are those that he has already in large measure observed and for which he would like an explanation.

The book begins with a description of the chromosomal material within eggs and sperm cells, of how it is transmitted to future generations and of how genes act to produce certain visible effects. Single and multifactor inheritance, the origin and significance of mutations, sex determination, and the consequences of consanguinity and miscegenation are discussed at length. At the end of the book are several chapters of extreme interest dealing with subjects to which the science of genetics has made a real contribution. These include heredity and environment, selection and engenics, aspects of race mixture, and the origin of human diversity.

The book is a remarkable combination of factual material and thought-provoking suggestions. It can be read with enjoyment as well as profit by anyone seeking a basis for understanding the physiologic and emotional behavior of mankind.   EDITH L. POTTER.

Human Procreation[4] by Belonoschkin is a comprehensive little monograph dealing with practically all phases of that subject. The book begins with a description of the structure, chemistry, motility, physical chemistry and metabolism of the spermatozoon. From this point the discussion is carried through all the anatomical structures which the male zygote must traverse to reach the ovum. The complete anatomy, biology, and chemistry of these organs are discussed.

As the title implies, the work is particularly complete in its treatment of the male generative tract and its products. Fully fifty pages are devoted to the characteristics of the ejaculate. In contrast, the chapter upon the ovum is very brief.

The illustrations are rather infrequent and lacking in clarity. In general, however, this is a thorough and valuable review of the masculine side of reproduction. The bibliography is complete and well organized, and the book should serve as a handy and complete reference for workers in that field.   BRUCE A. HARRIS, JR.

Because this book, **Human Fertility and Problems of the Male,**[5] has been publicized by the lay press, it requires particular appraisal. It must be understood at the start that it is not a general treatise on the fertility of the human male, but is an exposition of beliefs which are at present peculiar to the author. Two premises are implicit in his presentation, the first being that his rat ovary hyperemia test precisely determines the day of human ovulation, and the second being that his method for evaluating semen quality is supremely reliable. In medical science as in other logic, unless the premise is true and the reasoning sound, the conclusion will be incorrect. The hyperemia test may truly indicate ovulation, as Farris believes, but his findings have not been generally confirmed by other investigators, and the balance of critical comment thus far published has been unfavorable.

So much for the first premise which is passed over lightly, both by the author and reviewer. Now for the second. The essential contribution by the author is the idea that the total number of active spermatozoa in the entire ejaculate is the prime index of male fertility. Students of fertility have long been searching for just such a simple determinant. Since it has heretofore eluded them, one might expect of the author a full presentation of data and a solid exposition of facts which might lead the reader to conclude that he had found it. The volume contains the shadow, not the substance, of such a presentation. The reader lacks full data upon which to form his opinions and is thus obliged to accept the author's word for the validity of the premises. What of the logic? Surely there is something amiss with reasoning which leads to the conclusion that "20 per cent [of men in this country] will probably never become fathers," and, "another 35 to 40 per cent may never become fathers" (page 3), or the estimate that "about 60 per cent of those in the population who want children will have a fertility problem" (page 99).

Why is this work, taken as a whole, defective? There are many reasons, the first of which is his human material. Since the author is not a physician his clinical material (that is, infertile couples) must originally have been referred to him by physicians. It is obvious that they would not refer patients with curable organic disorders, such as endocervicitis, myomas of the uterus, ovarian cysts, vesiculitis, malnutrition, or the many other ailments which yield to therapy and, when cured, are often followed by fertility. Clinicians usually exhaust their own resources before referring patients to consultants, so that it is probable that the author has been dealing with a group of infertile couples who constitute the unsuccessful siftings from the offices of physicians.

Only by assuming that Farris is dealing with such a highly selected group can one understand how he could have reached conclusions which confute both clinical experience and

[4]**Zeugung beim Menschen im Lichte der Spermatozoenlehre.** By Boris Belonoschkin. From the Sperm Investigation Laboratory of the Woman's Clinic of the Karolinska Hospital in Stockholm, Sweden. 228 pages, 25 illustrations. Stockholm, 1949. Sjöberg's Förlag. Price, 20 Swedish Kroner ($3.86).

[5]**Human Fertility and Problems of the Male.** By Edmond J. Farris, Ph.D. 211 pages. $3.00. The Author's Press, Inc., publishers. White Plains, New York.

common sense. Second, the author has handled his data in a most reprehensible way. The reader is not presented with all the data, but only with isolated tabulations of scores or hundreds of patients from the thousand or so studied. Sweeping general conclusions are drawn, it appears, from miserably inadequate sample groups. Many of the tabulations are extremely difficult to interpret. The fragmentary data do not permit a satisfying statistical or biometric analysis. There is inadequate discussion of the failures or weaknesses, if any, in the author's methods. The success rate for infertile couples was 86 per cent for highly fertile husbands, 75 per cent for the relatively fertile, and 15 per cent for the subfertile. (One wonders whether an occasional wife might have been less than 100 per cent fertile.) The fact that these figures are two or three times as high as those submitted by the most reliable and experienced clinicians in the world suggests that Farris' material has been preselected, whether he realizes it or not. Finally, the impression grows upon the reader that the author is not writing as a scientist, fully assembling and objectively analyzing facts, but is actually a protagonist for his own methods.

Something should be said of the style of the book. At first glance it appears to be scientific; in a very limited sense it is. It is also startling—''20 to 25 per cent will probably never become fathers'' (page 3) or shocking—coitus interruptus ''may be performed in the laboratory'' (page 46), or astounding—''while he slept, the couple were able to consumate the act'' (page 188), but it is never oppressively modest.

The book is extremely difficult to review because its argument is more compelling than convincing and because the author has some brilliant ideas which are not sufficiently developed for appraisal. The preface states that the book was written in response to requests from physicians, scientists, and laymen. Those who read it will be, respectively, confused, amused, and bemused. In spite of a few excellent suggestions, some interesting thoughts, and much earnestly garnered data on sperm, this volume is not for the general physician or layman. It should be read only by the specialist in the study of infertility, for he alone will appreciate the author's originality and be able to digest his theories, many of which should have baked longer in the oven of experience. Evidently the publisher was aware of this for he warns that ''this book or any part thereof must not be reproduced.''   PENDLETON TOMPKINS.

In her monograph, ''**Haemolytic Disease of the Newborn,**''[6] M. M. Pickles presents the most complete coverage of this subject that has thus far been made available to the profession.

The many-angled approach to the topic makes the book a useful one not only to the hematologist and laboratory worker but also to the clinical obstetrician and pediatrician. The content of material is extensive though concise, and brings the reader as nearly up to date with the subject as is possible in any problem upon which so much investigative effort is being expended.

The reader will find an introduction dealing quite fully with the evolution of knowledge of disease and appropriate bibliography. This is followed by chapters on the nature of the Rh antibodies, the correlation of old and new nomenclatures, the relation of the Rh and other blood groups to hemolytic disease, the mechanism of immunization, the patterns of pathology, treatment, and sequelae.

The importance of the subject and the clear, complete manner in which it has been handled make this a most desirable reference volume for those who have contact, in one direction or another, with the disease.   THADDEUS L. MONTGOMERY.

This book, **Fertility in Marriage,**[7] is designed to inform laymen of the causes of infertility, the methods of clinical investigation, the rationale of therapy, and the chances of

[6]**Haemolytic Disease of the Newborn.** By M. M. Pickles, Nuffield Graduate Assistant in Clinical Pathology, Radcliffe Infirmary, Oxford. 181 pages with 21 figures and 19 charts. Springfield, Ill., 1949., Charles C Thomas.

[7]**Fertility in Marriage.** By Louis Portnoy, M.D., and Jules Saltman. 250 pages, 2 illustrations. New York, 1950. Farrar, Straus and Company, Inc., $3.00.

success. The material is well arranged in twenty chapters beginning with, ''When to start wondering'' and ''Where to seek help,'' and passing to discussion of the mechanism of conception, the anatomic and physiologic requirements, the studies required to verify their normality, to the prognosis, and finally, to artificial insemination and adoption. The authors' tone of conservatism and their emphasis upon patience are particularly commendable. Even such debatable measures as irradiation for anovulation are handled with wisdom and finesse. Since this book is for the layman there is no bibliography, but due credit is given to those who have notably advanced infertility studies. Two appendices provide addresses of ''Infertility Clinics'' and adoption agencies. The writing is simple, pleasant, and always dignified. The book will save much time for the busy clinician who recommends it to his infertile patients, because the general problems are discussed in greater detail than he can regularly provide. The volume can be recommended without reservation to infertile couples, to physicians who treat them, and to any physician who wishes to review modern methods in this subspecialty of gynecology and urology. It is excellent.   PENDLETON TOMPKINS.

Correspondence

Trichomonas Vaginalis

To the Editor:

The paper of Hundley and associates on "Trichomonas Vaginalis Vaginitis: Treatment With a New Surface-Active Trichomonacide" in the October issue of the JOURNAL was read with a great deal of interest because we have been studying *Trichomonas vaginalis* continuously for the past eighteen years.

In one sentence Hundley states "since *Trichomonas vaginalis* grows luxuriantly in acid secretions, obviously efforts to maintain an acid pH of the vagina are not of great value." This statement aroused my curiosity since we were the originator of acid treatment for vaginal infections. It was shown by us years ago that *Trichomonas vaginalis* would not grow in a pH below 5.0 and this author quotes from the monograph on *Trichomonas vaginalis* by Dr. Trussel where he states, on page 29 of the book, "The maximum population developed between pH 5.5 and pH 6.0. No growth occurred below pH 5.0 or above pH 7.5." The fact that the trichomonads grow luxuriantly in a weak acid medium of pH 5.5 bears no relationship to what the organisms would do in a highly acid pH of 3.0. We have tested most acids known today and found that as long as the vagina is kept at pH around 4.0 no trichomonads lived and we came to a dictum found in our textbook *Practical Office Gynecology*, on page 143, "Any acid preparation, pH 2.9 to 4.5, can be used, since it is the pH (acidity) of the drug rather than any constituent in the chemical that destroys *Trichomonas vaginalis*." It appears to me that we might assume in a similar manner that because a man could bathe in warm water that he could also bathe in boiling water. To me that is synonymous with Dr. Hundley's statement that because trichomonads live in a weak acid medium they can live in any acid medium regardless of how strongly acid it is.

A good trichomonacide is still needed because up to the present all drugs so far on the market have been tried in the Leucorrhea Clinic which I have been conducting for years and we have found that trichomonads are not destroyed in many cases. The addition of this drug may be another chemical for the treatment of *Trichomonas vaginalis* because one drug may not be of value but when another is used Trichomonas is eradicated. We are at present studying many chemicals in vaginas infected with trichomonads.

Another question we could raise about the paper is that 73 of these cases were reported negative in 1 week and 90 within 2 weeks and 94 within 4 weeks. We were of the opinion that a patient is said to be negative for *Trichomonas vaginalis* when she has not douched for at least one month and comes back the day after the third menstrual cycle and no *Trichomonas vaginalis* is found in the vaginal secretion. No vaginal douche is taken the day that she comes for a check-up.

Most drugs will kill trichomonads in the test tube very easily, but when applied to the vagina many other factors appear to come into play. After applying most drugs advocated one can find trichomonads swimming in the media mixed with the vaginal secretion and in 3 to 4 days after the drug is discontinued trichomonads are usually found in the vagina.

The question of Trichomonas in the male is not even brought up and it is generally known that the male is the carrier of the Trichomonas.

Personally I would like to have other efficient preparations for *Trichomonas vaginalis*, but we have certainly found out in years of experimental work in thousands of cases of *Trichomonas vaginalis* that the lower the pH of a drug the better the final results.

Efforts to maintain an acid pH of the vagina are of great value in the treatment of *Trichomonas vaginalis* and most infections of the vagina.

KARL JOHN KARNAKY, M.D.

329 MEDICAL ARTS BUILDING
HOUSTON, TEXAS
NOVEMBER 15, 1950

Reply by Dr. Shelanski

To the Editor:

In reference to the above letter from Dr. Karnaky, may we state that there is no excuse for any medical man to submit a criticism full of half-truths and inaccuracies, especially since Dr. Karnaky claims to have been studying *Trichomonas vaginalis* continuously for the past eighteen years.

First of all, Dr. Karnaky claims to be the originator of the acid treatment for vaginal infection. Yet in the literature there are references which pre-date Dr. Karnaky's birth by at least fifty years. I have in mind Von Kolliker and H. V. Scanzoni's paper in 1855, entitled "Das Sekret der Schleimhaut der Vagina und des Cervix Uteri," which refers to an acid treatment of Trichomonas infections.

Second, Dr. Karnaky states that, according to his work, *Trichomonas vaginalis*, would not grow in a medium of pH below 5.0. To confirm his work he quotes Dr. Trussel's monograph (page 29), "The maximum population developed between pH 5.5 and 6.0. No growth occurred below pH 5.0 or above pH 7.5." What Dr. Karnaky neglected to point out was the fact that these results were obtained on pure cultures of *Trichomonas vaginalis*. The pH of cultures containing both bacteria and *Trichomonas vaginalis* has a wider range. Dr. Trussel, on the same page quoted by Dr. Karnaky, states that Westphal in 1936 obtained a growth of Trichomonas in a pH range of 4.0 to 8.8 in the presence of contaminating bacteria. Also the writer in a Master's dissertation (available at the University of Pennsylvania library) showed that *Trichomonas vaginalis* may be adapted to an alkaline medium containing Loeffler's dehydrated blood serum as well as to an acid medium in cultures containing Bacto-liver infusion. The pH of these cultures ranged between 4.0 and 8.6. Does Dr. Karnaky believe that the Trichomonas infection of the vagina is unaccompanied by contaminating bacteria, and, if so, has he ever obtained pure cultures of *Trichomonas vaginalis* without bacteria from patients suffering from *Trichomonas vaginalis* vaginitis?

Third, Dr. Karnaky states that he has tested most acids known today and found that as long as the vagina is kept at pH 4.0, no trichomonads lived, and he came to a dictum found in his textbook, *Practical Office Gynecology*, on page 43, "Any acid preparation, pH 2.9 to 4.5 can be used, since it is the pH (acidity) of the drug rather than any constituent in the chemical that destroys *Trichomonas vaginalis*." We would be willing to question whether Dr. Karnaky has actually used "most acids known today" in his investigation, there being several thousand chemicals possessing acid properties. In addition, does he believe that the lethal effect of all acids including nitric acid, cyanic acid, etc., is exerted mainly through the hydrogen ion concentration? Is he willing to ignore the fact that chemicals, whether acid or not, may have an inherent toxic property?

Fourth, the comparison between the effects of pH and boiling water is utterly incongruous. We did not state that "because Trichomonads live in a weak acid medium, they can live in any acid medium regardless of how strongly acid it is." We merely wished to emphasize that Trichomonads can survive in a wide pH range. This range includes the pH which Dr. Karnaky attempts to establish in the vagina by means of his acid treatments. We are sure that, if the pH of the vagina could be maintained comfortably at 1.0 to 3.0, the Trichomonads would not survive. But would Dr. Karnaky advise

any attempt to establish such a pH? It is well known that vaginal infections of *Trichomonas vaginalis* may occur in conjunction with Monilia, the latter organism requiring a medium maintaining a pH of 3.0 to 4.0.

We agree with Dr. Karnaky on one point, namely that a good trichomonacide is still needed. We have investigated the use of Tetronyl for that very purpose. We think that our results justify the use of this substance in the treatment of *Trichomonas vaginalis* vaginitis. Although this substance is buffered to maintain a pH of between 4.0 to 4.5, we do not claim that this in any way alters the pH of the contents of the vagina to that range. The very fact that Trichomonads can survive in bacteria-contaminated media at that range would preclude our claiming that it is the pH which is responsible for the good results obtained in our investigation. On the other hand there must be some inherent protozoacidal effect of the compound which is responsible for its action.

Dr. Karnaky questions our results because he is of the opinion that a patient "is said to be negative for *Trichomonas vaginalis* when she has not douched for at least one month and comes back a day after the third menstrual cycle and no *Trichomonas vaginalis* is found in the vaginal secretion. No vaginal douche is taken the day she comes for a check-up." This standard for a cure was established by the writer and his group many years ago and is the same standard followed in this study.

Once more, Dr. Karnaky tells us that the subject of Trichomonas in the male has not been brought up in the discussion. If he will look on page 847, paragraph 6, he will find that this point is also discussed, or is he attempting to criticize the paper without having become acquainted with its contents?

In conclusion, the authors have investigated a drug which we feel is indicated in the treatment of Trichomonas infection of the vagina and we welcome constructive criticism of this treatment, but, until Dr. Karnaky can furnish us with scientific proof of his statements, and until he has tried our treatment himself, he is in no position to judge or analyze our procedures merely because he has a pH-ax to grind.

HERMAN A. SHELANSKI, PH.D.

PHILADELPHIA, PA.
NOVEMBER 21, 1950.

Necrology

ROBERT LATOU DICKINSON, M.D., clinician, teacher, artist, author, died in Amherst, Mass., on Nov. 29, 1950, after a long illness, at the age of almost ninety. Born in Jersey City, N. J., Feb. 21, 1861, he studied at the Brooklyn Polytechnic, then in Switzerland and Germany, before receiving his M.D. degree at the Long Island College in 1882, where later he became professor of obstetrics and gynecology as well as chief of service at the Brooklyn Hospital. He retired in 1924 and devoted himself to the study of human fertility. Dr. Dickinson was a prolific writer and illustrated his numerous books and articles with a facile pen, creating a now well-known style of drawing. He was the first physician of prominence to advocate voluntary birth control, urging its scientific practice by the profession, and was active in the development of the Planned Parenthood Association. During World War I he served as assistant chief of the medical section of the National Council of Defense and was commissioned a lieutenant colonel in the Army Medical Corps, developing standards for the hospital care of returning veterans.

A founder of the American College of Surgeons, a member of numerous medical societies, a Fellow of the American Gynecological Society and its President in 1920, his address as President constituted the first article in the initial number of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY of which he was a member of the Advisory Editorial Board since the founding in 1920. The JOURNAL was indebted to him for the interesting drawings of the various title pages of its successive anniversary issues, the last appearing in the recent Thirtieth Anniversary Issue published in November.

For many years Dr. Dickinson was a leading member of the medical profession; he was an active participant in the advances made in the specialty during the past half century; by his works and deeds he established his fame as a physician, as a writer, and as an artist.

Items

American Board of Obstetrics and Gynecology

The next scheduled examination (Part I), written examination and review of case histories, for all candidates will be held in various cities in the United States and Canada on Friday, Feb. 2, 1951. Arrangement is being made for proctors in locations convenient to the candidates' places of practice.

Candidates who have already successfully completed Part I and who desire to reopen their applications for Part II examinations may do so by notification to this office until Feb. 2, 1951.

The next oral and pathology examination (Part II) will be held at The Waldorf-Astoria Hotel, New York City, from May 10 to 16, inclusive, 1951.

For new Bulletins or other information address:

> PAUL TITUS, M.D., Secretary
> American Board of Obstetrics and Gynecology
> 1015 Highland Building
> Pittsburgh 6, Pa.

Thirteenth British Congress of Obstetrics and Gynaecology

The Thirteenth British Congress of Obstetrics and Gynaecology will be held at Leeds, Yorkshire, on July 8, 9, 10, and 11, 1952.

The subjects for discussion are:

Abnormal Uterine Action in Labour

Stress Incontinence of Urine

The Place of the Paediatrician in a Maternity Unit

Genital Tuberculosis in the Female

All communications relating to this Congress should be addressed to the Secretary, B. L. Jeaffreson, M.D., 32, Park Square, Leeds, 1, England.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. (1876) *President*, Frederick C. Irving. *Secretary*, Norman F. Miller, 1313 East Ann St., Ann Arbor, Mich. Annual meeting, May 7, 8, 9, 1951, New York City.

American Association of Obtetricians, Gynecologists and Abdominal Surgeons. (1888) *President*, James K. Quigley, Rochester, N. Y. *Secretary*, William F. Mengert, 2211 Oak Lawn Ave., Dallas 4, Texas. Annual meeting Hot Springs, Va., September 6, 7, and 8, 1951.

Central Association of Obstetricians and Gynecologists. (1929) *President*, Russell J. Moe, Duluth, Minn. *Secretary-Treasurer*, Harold L. Gainey, 116 S. Michigan Ave., Chicago 3, Ill. Annual meeting to be held in September, 1951.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President*, Lester A. Wilson, Charleston, S. C. *Secretary-Treasurer*, John C. Burwell, Jr., 416 Jefferson Bldg., Greensboro, N. C. Annual meeting, Ormond Beach Hotel, Ormond Beach, Florida, Feb. 8, 9, and 10, 1951.

A. M. A. Section on Obstetrics and Gynecology. *Chairman*, James R. Blos, Huntington, W. Va. *Secretary*, A. B. Hunt, Mayo Clinic, Rochester, Minn. Annual meeting June, 1951, Atlantic City, N. J.

New York Obstetrical Society. (1863) *President*, Howard C. Taylor, Jr. *Secretary*, Charles M. McLane, 960 Park Ave., New York 28, N. Y. Second Tuesday, from October to May.

Obstetrical Society of Philadelphia. (1868) *President*, James P. Lewis. *Secretary*, George A. Hahn, 255 S. 17th St., Philadelphia, Pa. First Thursday, from October to May.

Chicago Gynecological Society. (1878) *President*, John I. Brewer. *Secretary*, Edward M. Dorr, 30 N. Michigan Ave., Chicago 2, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. (1890) *President*, Martin Shir. *Secretary*, J. Edward Hall, 429 Clinton Avenue, Brooklyn 5, N. Y. Third Wednesday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.

Baltimore Obstetrical and Gynecological Society. (1929) *President*, Houston S. Everett. *Secretary-Treasurer*, W. Drummond Eaton, 11 E. Chase St., Baltimore 2, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.

Cincinnati Obstetrical Society. (1876) *President*, Edward Friedman. *Secretary*, Robert R. Pierce, 116 William Howard Taft Road, Cincinnati 19, Ohio. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President*, Rudy F. Vogt. *Secretary-Treasurer*, Glenn W. Bryant, Louisville, Ky. Meetings fourth Monday of each month from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. *President*, William Sharkey. *Secretary-Treasurer*, Jack W. Dowsett, 1020 S. W. Taylor St., Portland 5, Ore. Meetings last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President*, Eugene A. Conti. *Secretary-Treasurer*, David Katz, 103 Century Bldg., Pittsburgh 22, Pa. Meetings, first Monday of each month, October to May.

Obstetrical Society of Boston. (1861) *President*, Roy J. Heffernan. *Secretary*, Francis Rouillard, 1180 Beacon Street, Brookline, Mass. Third Tuesday, October to April, Harvard Club.

New England Obstetrical and Gynecological Society. (1929) *President*, Arthur E. G. Edgelow, Springfield, Mass. *Recorder*, Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President*, Philip H. Arnot. *Secretary-Treasurer*, R. Glenn Craig, 490 Post St., San Francisco, Calif.

Washington Gynecological Society. (1933) *President*, J. Bay Jacobs. *Secretary*, Allan E. King, 915 19 Street, N.W., Washington, D. C. Fourth Saturday, October, November, January, March, May.

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*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the Society's name is the year of founding.

New Orleans Obstetrical and Gynecological Society. (1924) *President*, John Herring. *Secretary*, E. W. Nelson, 1407 S. Carrollton Ave., New Orleans, La. Meetings held October, November, January, March, and May.

St. Louis Gynecological Society. (1924) *President*, T. K. Brown. *Secretary*, J. Russell Vaughan, 634 North Grand Blvd., St. Louis 3, Mo., Regular meetings second Thursday, October, December, February, and April.

San Francisco Gynecological Society. (1929) *President*, Donald Dallas. *Secretary*, Donald W. de Carle, 2000 Van Ness Ave., San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. (1930) *President*, Howard O. Smith, Marlin, Texas. *Secretary*, George F. Adam, 4115 Fannin St., Houston 4, Tex.

Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President*, O. W. Picard. *Secretary*, Carl F. Shelton, 910 David Broderick Tower, Detroit 26, Mich. Meetings first Tuesday of each month from October to May (inclusive).

Central New York Association of Gynecologists and Obstetricians. (1938) *President*, Nathan N. Cohen. *Secretary*, Merton C. Hatch, Medical Arts Bldg., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.

Alabama Association of Obstetricians and Gynecologists. (1940) *President*, M. Y. Dabney. *Secretary*, Buford Word, 929 South Twentieth Street, Birmingham, Ala.

San Antonio Obstetric Society. *President*, I. T. Cutter. *Secretary*, S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.

Seattle Gynecological Society. (1941) *President*, Robert K. Plant. *Secretary-Treasurer*, Gerald F. Thomas, 1427 Medical and Dental Bldg., Seattle 1, Wash. Meetings held on third Wednesday of each month, Washington Athletic Club.

Denver Gynecological and Obstetrical Society. (1942) *President*, Edward L. Harvey. *Secretary-Treasurer*, Jack M. Simmons, Jr., 804 Republic Bldg., Denver 2, Colo. Meetings held first Monday of every month from October to May (inclusive).

Wisconsin Society of Obstetrics and Gynecology. (1940) *President*, J. W. Prentice. *Secretary-Treasurer*, Alice D. Watts, 324 East Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.

San Diego Gynecological Society. (1937) *President*, D. Dalton Deeds. *Secretary*, Jesse A. Rust, Jr., 3115 University Ave., San Diego 4, Calif. Meetings held on the last Friday of each month.

North Dakota Society of Obstetrics and Gynecology. (1938) *President*, W. H. Gilsdorf, Valley City. *Secretary-Treasurer*, C. B. Darner, Fargo, N. D.

Virginia Obstetrical and Gynecological Society. (1936) *President*, John M. Nokes. *Secretary*, Chester D. Bradley, 2914 West Avenue, Newport News, Va. Meetings held in April and October.

Columbus Obstetric and Gynecologic Society. (1944) *President*, Wayne Brehm. *Secretary*, Zeph J. R. Hollenbeck, 9 Buttles Ave., Columbus, Ohio. Meetings held fourth Wednesday of each month.

Naussau Obstetrical Society. (1944) *President*, Robert S. Millen. *Secretary-Treasurer*, Peter La Mariana, Williston Park, L. I., N. Y. Meetings, bimonthly from October to May.

Bronx Gynecological and Obstetrical Society. (1924) *President*, Charles W. Frank. *Secretary*, Benjamin Karen, 1100 Grand Concourse, New York 56, N. Y. Meetings, fourth Monday monthly from October to May.

Washington State Obstetrical Society. (1936) *President*, Charles Kimball. *Secretary-Treasurer*, E. Gerald Layton, 805 Medical and Dental Bldg., Seattle 1, Wash. Meetings first Saturday in April and second Saturday in September.

Kansas City Obstetrical and Gynecological Society. (1922) *President*, Richard B. Schutz. *Secretary*, William C. Mixson, 320 W. 47th St., Kansas City, Mo. Meetings, last Thursday, September, November, January, and March; first Thursday, May, University Club.

Los Angeles Obstetrical and Gynecological Society. (1914) *President*, A. M. McCausland. *Secretary-Treasurer*, Gordon Rosenblum, 6333 Wilshire Blvd., Los Angeles 36, Calif.

North Carolina Obstetrical and Gynecological Society. (1932) *President*, Wallace B. Bradford. *Secretary*, Richard B. Dunn. Meetings semiannually.

The Society of Obstetricians and Gynecologists of Canada. (1944) *President*, H. B. Atlee. *Secretary*, K. M. Grant. Annual meeting, June, 1950.

Akron Obstetrical and Gynecological Society. (1946) *President*, H. H. Gibson. *Secretary-Treasurer*, E. A. Riemenschneider, Second National Bldg., Akron 8, Ohio. Meetings held third Friday of January, April, July, and October, City Club of Akron, Ohio Bldg.

Minnesota Obstetrical and Gynecological Society. *President*, James Swendson. *Secretary-Treasurer*, John A. Haugen, 100 East Franklin, Minneapolis 4, Minn. Meetings held spring and fall.

Miami Obstetrical and Gynecological Society. (1946) *President*, Homer L. Pearson. *Secretary*, John D. Milton, 1104 Huntington Bldg., Miami, Fla. Meetings, second Thursday in January, March, May, and November.

Omaha Obstetrical and Gynecological Society. (1947) *President*, Ralph Luikhart. *Secretary-Treasurer*, Donald C. Vroman, 813 Medical Arts Bldg., Omaha 2, Neb. Meetings held third Wednesday in January, March, May, September, November.

Oklahoma City Obstetrical and Gynecological Society. (1940) *President*, John W. Records. *Secretary-Treasurer*, Henry G. Bennett, Jr., 800 Northeast 13 Street, Oklahoma City 4.

Cleveland Obstetrical and Gynecological Society. (1947) *President*, J. L. Reycraft. *Secretary*, G. Keith Folger, 10515 Carnegie Ave. Meetings on fourth Tuesday of September, November, January, March, and May at University Club, 3813 Euclid Ave., Cleveland 15, Ohio.

New Jersey Obstetrical and Gynecological Society. (1947) *President*, J. Carlisle Brown. *Secretary*, Harold Schwartz, 201 Lyons Ave., Newark 8, N. J. Meetings semiannually.

Honolulu Obstetrical and Gynecological Society. (1947) *President*, Guy C. Milnor. *Secretary*, Rodney T. West, The Clinic, Honolulu 14, T. H. Meetings third Monday of each month, Mabel Smyth Building.

Oregon Society of Obstetricians and Gynecologists. *President*, Gerald Kinzel. *Secretary-Treasurer*, Theodore M. Bischoff, 529 Mayer Bldg., Portland 5, Ore. Meetings held on third Friday of each month from October to May.

National Federation of Obstetric-Gynecologic Societies. (1945) *President*, Ralph E. Campbell. *Secretary*, Woodard D. Beacham, 429 Hutchinson Memorial Bldg., New Orleans 13, La.

Dayton Obstetrical and Gynecological Society. (1937) *President*, C. E. Mumma. *Secretary*, N. J. Thompson, 610 Harries Bldg., Dayton 2, Ohio. Meetings, third Wednesday monthly from September through June at the Van Cleve Hotel.

Dallas-Fort Worth Obstetric and Gynecologic Society. (1948) *President*, Asa A. Newsom. *Secretary*, A. W. Diddle, 2211 Oak Lawn Ave., Dallas 4, Texas. Meetings in spring and fall.

Queens Gynecological Society. (1948) *President*, Frederick Carpenter. *Secretary*, George Schaefer, 112-25 Queens Blvd., Forest Hills, N. Y. Meetings held second Wednesday in February, April, October, and December, at the Queens County Medical Society Bldg.

Mississippi Association of Obstetricians and Gynecologists. (1947) *President*, R. C. O'Ferrall. *Secretary*, William Weiner, Barnett-Madden Bldg., Jackson, Miss. Meetings held semiannually.

Florida Obstetric and Gynecologic Society. (1948) *President*, Robert G. Spicer. *Secretary-Treasurer*, Dorothy D. Brame, 1235 Kuhl Ave., Orlando, Fla. Next annual meeting, April, 1951, at Hollywood, Fla.

South Carolina Obstetrical and Gynecological Society. (1946) *President*, J. Decherd Guess. *Secretary*, Arthur L. Rivers, 231 Calhoun St., Charleston, S. C. Meetings held in spring and fall.

Buffalo Obstetrical and Gynecological Society. (1946) *President*, W. Herbert Burwig. *Secretary*, Clyde L. Randall, 925 Delaware Avenue, Buffalo, N. Y. Meetings held on the first Tuesday of October through May at the Saturn Club.

El Paso Gynecological Society. (1948) *President*, Gerald H. Jordan. *Secretary-Treasurer*, Gray E. Carpenter, 303 N. Oregon St., El Paso, Texas.

Kentucky Obstetrical and Gynecological Society. (1947) *President*, A. J. Whitehouse. *Secretary*, Edwin P. Solomon, 910 Heyburn Bldg., Louisville, Ky.

Indianapolis Obstetrical and Gynecological Society. (1947) *President*, David L. Smith. *Secretary*, Sprague H. Gardiner, 314 Hume Mansur Bldg., Indianapolis 4, Ind. Meetings held in January, April, and October.

Houston Obstetrical and Gynecological Society. (1939) *President*, John A. Wall. *Secretary-Treasurer*, Herman L. Gardner, Hermann Professional Bldg., Houston 5, Texas. Meetings held second Tuesday of each month except July, August, and September.

Iowa Obstetric and Gynecologic Society. *President*, J. H. Randall. *Secretary*, William C. Keettel, Iowa City, Iowa.

Memphis Obstetrical and Gynecological Society. (1950) *President*, Phil C. Schreier. *Secretary*, James H. Smith, 1665 Madison Ave., Memphis 4, Tenn. Meetings, fourth Friday, October to May.

Birmingham Obstetrical and Gynecological Society. (1949) *President*, W. N. Jones. *Secretary*, Herbert H. Thomas, 1005 South Twenty-First St., Birmingham, Ala. Meetings four times yearly.

Mobile Obstetrical and Gynecological Society. (1949) *President*, John C. Hope, Jr. *Secretary*, Virginia E. Webb, 1322 Springhill Ave., Mobile, Ala. Meetings held second Thursday of January, April, July, and October.

Utah Obstetrical and Gynecological Society. (1948) *President*, William M. Nebeker. *Secretary*, Vernal H. Johnson, 2279 Jackson Ave., Ogden, Utah. Meetings held second Thursday of October, December, March, and May, at the University Club, Salt Lake City.